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PRETRAUMATIC PERSONALITY AND PSYCHIATRIC SEQUELAE OF HEAD INJURY

II. Correlation of Multiple, Specific Factors in the Pretraumatic Personality and Psychiatric Reaction to Head Injury, Based on Analysis of One Hundred and One Cases

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THIS paper is a study of the relationship between multiple specific factors in the pretraumatic personality and the psychiatric sequelae of head injury.

In part I [1] of the study I presented the results of a correlation of the categorical pretraumatic personality and the general psychiatric reaction to head injury of 200 patients. Each patient in that series had been given a categorical classification of the pretraumatic personality under one of the following ten headings:

Normal personality
Psychopathic personality
Neurotic personality
Personality variant
Normal personality except for general nervousness
Mental deficiency
Neurotic traits in childhood
Behavior problem (childhood and youth)
Psychotic behavior
Pretraumatic personality unknown

Comprehensive personality classification is common practice in psychiatry, as in general medicine and neurology. It was recognized,

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1. Kozol, H. L.: Pretraumatic Personality and Psychiatric Sequelae of Head Injury: I. Categorical Pretraumatic Personality Status Correlated with General Psychiatric Reaction to Head Injury Based on Analysis of Two Hundred Cases, Arch. Neurol. & Psychiat. **53**:358-364 (May) 1945.

however, that such a general personality classification might be inadequate in contributing information regarding the etiologic factors in the psychiatric sequelae of head injury. In part I [1] the pretraumatic personality types were correlated with the following post-traumatic psychiatric phenomena:

Anxiety states
Fatigue (neurasthenia syndrome)
General nervousness
Hypochondriasis
Obsessive-compulsive-phobic states
Depressive states
Euphoria

It was found that 64 out of the 200 patients showed one or more of these symptoms, each of which had been explicitly defined in keeping with general psychiatric usage.

It was concluded:

> . . . there is little, or no, correlation between [categorical] pretraumatic personality and the liability to development of post-traumatic mental symptoms. A patient with a pretraumatic "neurotic" personality may be free from symptoms. A patient with a pretraumatic "normal" personality may be crippled by mental symptoms. This does not mean that the pretraumatic personality may not play a large, or even the sole, part in the production of post-traumatic mental symptoms. It does mean that the development of post-traumatic mental symptoms may not generally be ascribed to the pretraumatic personality. There is no general rule that patients with over-all neurotic or psychopathic personalities are more likely to manifest symptoms after trauma than are normal persons.

It was further concluded that there is "a significant correlation between the incidence of post-traumatic mental symptoms and the existence of complicating psychosocial factors," such as the persistence of associated bodily injuries, occupational stresses, marital difficulties and pending litigation or continuing compensation.

In the present study, which dealt with every other patient in the previous study, a more intensive investigation was made of multiple, specific factors in the personality, both before and after head injury. It was recognized that categorical classification might overlook factors which might be present in various personality groups. It was felt, furthermore, that the number of post-traumatic psychiatric phenomena dealt with in the previous study might be inadequate in giving a picture of the psychiatric reaction to head injury. The observations in the present study are also correlated with categorical personality classifications. Finally, this study embraces correlations with the nature and severity of the head injury, as such, and the existence of complicating psychosocial factors, in an attempt to elucidate the psychiatric sequelae of head injury.

MATERIAL

The 101 patients on whom this study was based represent approximately one half of a group of 200 subjects of a comprehensive investigation of civilian head injuries conducted at the Boston City Hospital from July 1942 to October 1944, under the direction of Dr. D. Denny-Brown, who has already presented a summary of the results of that study.[2] These patients had been selected from a series of 430 persons with acute head injuries who had been admitted to the hospital immediately after injury, by exclusion of persons under 15 and over 55 years of age and of vagrants, irresponsible and unemployed alcohol addicts, chronically unemployed persons and patients on whom follow-up studies were unobtainable. In the present study, 2 patients with chronic alcoholism were included because of the gross severity of their head injuries and the fact that they had histories of some work dependability. Of the 101 patients in this study, 66 were males and 35 were females. Eight patients were between 15 and 20 years of age; 26 were between 20 and 29; 20 were between 30 and 39; 31 were between 40 and 49; 12 were between 50 and 55, and 4 were over 55. Seventy per cent of the patients were under the age of 46. With but few exceptions, these patients had been selected at random in that every other patient admitted was selected for the present study, in addition to the regular study described in part I. The minimal period of observation was six months unless the patient showed freedom from symptoms previous thereto. Approximately 20 per cent of these patients were followed for more than one year, and some have been followed longer. Each patient underwent at least three detailed examinations after discharge from the hospital. The examinations took place at intervals of six weeks, three months and six months after discharge but in some instances were more frequent and in some cases were continued up to nine and twelve months after discharge.

METHOD

In order to evaluate psychologic factors in sequelae to head injury, one must have a base line. That base line is the pretraumatic personality. By reference to the pretraumatic personality one can determine whether there has been a change since the head injury.

The necessity of establishing a personality base line resulted in my adherence to the historical-biographic method of personality study. I wished to know what sort of a person the patient was before he had been injured. It was obvious that a history of the patient's actual performances and experiences in certain situations would provide the most dependable basis for judgment. This is the classic psychiatric case history. This method is open to various criticisms. It goes without saying that the history may not cover enough ground or be sufficiently penetrating. It was sought to make the histories as accurate as possible by checking the initial history at subsequent examinations of the patient, by interviews with relatives and by information obtained from various other sources by a social worker. This method of getting information about the patient's personality is tedious and time consuming. A short cut would have been welcomed; but in the present state of knowledge of human nature I know of no adequate substitute for a painstaking, detailed history of the patient's "past performances and experiences in their special settings."[1]

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2. Denny-Brown, D.: Disability Arising from Closed Head Injury, J. A. M. A. **127**:429-436 (Feb. 24) 1945.

As none of these patients had ever been given any formal personality tests, such as the Minnesota or the Rohrschach test, before the head injury, there was no logic in giving such tests after the injury because there was no basis for comparison. With what could a patient's post-traumatic reaction to ink blots be compared?

In general psychiatric history recording, information which has been obtained in the course of prolonged interviews with patients is often lost in the lengthy descriptions and reports of the conversations. To get around that, a master work sheet was devised. This work sheet includes a list of 60 items, most of which are descriptive of personality traits, tendencies or characteristics. The full list follows:

Work record unsteady
Steady, few jobs
Steady, many jobs
Alcoholism
  At time of injury
  Chronic
  Periodic
Asocial attitude (delinquent, criminal)
Timorousness
Prudence
Recklessness
Aggressiveness
Ambitiousness
Responsibility
Irresponsibility
Gaiety
Euphoria
Seriousness
Depressive state
Gregariousness
Seclusiveness
Egocentricity
Introspectiveness
Altrocentricity
Extrospectiveness
Sensitiveness
"Schizoid" attitude
Restlessness
Tenseness
Irritability
Excitability
Emotional stability
Emotional unstability
Emotional incontinence
Impulsiveness
Fatigability
Apathy
Abulia
Obsessive-compulsive-phobic state
Hypochondriasis
Anxiety, chronic
Anxiety attacks
Anxiety
  re head
  re family
  re occupation
  re other matters
Hysteria (conversion dissociation)
Sex disturbances
Insomnia
Fitful sleep
Increased need of sleep
Nightmares
Dreams (of accident)
Difficulties in concentration and memory
Headache
  Steady
  Periodic
Dizziness
Vertigo
Palpitation
Hyperhidrosis
Gastrointestinal disturbances

This list of items was selected arbitrarily by me. No claim is made that it encompasses every possible trait or deviation of personality. "Personality" is the sum total of one's tendencies, trends, capacities, liabilities, sensitivities and modes of reaction. Obviously, a complete list of all such possibilities would be nearly interminable and would, in fact, exceed any available vocabulary. In the interests of practicality, therefore, the list had to be rather arbitrarily limited. On

the basis of my experience, it appeared to me that the list selected was adequate and workable and that it embraced a sufficient number of significant items. The object of the use of this list was to provide a series of subjects for the uniform and controlled psychiatric examinations of these patients. The patients in this study came from all walks of life but mainly from the laboring, and even less privileged, classes. Some were earnest, steady citizens; others were indolent, alcoholic, irresponsible and even criminal. No rigid test could have been uniformly applicable to such a heterogeneous group which included persons of both sexes and of ages from 15 to 55 years (and beyond). With the use of a list of items as a guide, all patients were given substantially the same examination. Each item was used as the basis of special questions, each tailored to the particular background of the patient under examination. No arbitrary set of questions could have been generally applicable to this group of patients. It was necessary to adapt the examination to the patient.

It is thus obvious that this examination was not of the check sheet type. Despite the fact that patients were graded with respect to the strength of these items, all judgments were based on classic clinical psychiatric investigations. The list was simply a schema for uniformity of examination and recording in order to encompass a representative collection of traits, tendencies, characteristics, foibles, symptoms and complaints.

It will be noted that the list contains some items which may not ordinarily be included in considerations of personality. Thus, the first three items in the list refer to the patient's work habits. It must be conceded that consideration of such items offers considerable objectivity concerning the subject's makeup. The next three items deal with questions of alcoholism. The principal criticisms may be leveled against the inclusion of the last seven items in the list. These concern the presence of headaches, whether steady or periodic, and of dizziness, vertigo, palpitation, hyperhidrosis and gastrointestinal disturbances. They were included because, as they are common sequelae of head injury, it was deemed important to ascertain whether they existed before head injury. A further reason for including them was that this entire list was used as a schema for post-traumatic definition of the personality status. It appeared desirable, therefore, to include these items of a somatic class in order to avoid any assumptions as to whether they were due to organic lesions of the brain as such or were psychologic reactions to the trauma.

Most of the items in the list are familiar to psychiatrists. While it was desirable to avoid using words or terms which tended to beg questions by appearing too finalistic or diagnostic, it appeared desirable to include such terms as "schizoid," "obsessive," "compulsive," "hysterical" and "hypochondriacal." These terms were used not to indicate syndromes but, rather, to denote types of symptoms. Thus, "schizoid" does not indicate schizophrenia but, rather, designates oddity of personality in the sense of detachment from warm social rapport. The patient's attitude toward society and other persons appeared particularly relevant, as were also matters relating to his emotional balance and, particularly, his susceptibility to states of anxiety. The last item was considered under various subdivisions. Thus, a distinction was made between the occurrence of circumscribed attacks of anxiety and chronic states of anxiety. In addition, specific anxiety relating to the head was included because of Schilder's statement that such concern played a large part in the genesis of post-traumatic neurotic states.[3]

3. Schilder, P.: Neuroses Following Head and Brain Injuries, in Brock, S.: Injuries of Skull, Brain and Spinal Cord, Baltimore, William Wood & Company, 1940.

Psychopathy and normality are not mutually exclusive; they involve quantitative, as well as qualitative, factors. On the basis of such a premise, each item in the list of traits was quantitated clinically on a scale of 0 to 3. Where possible, quantitation is always desirable. However, the accuracy of quantitation is often limited by the nature of the subject matter. It was felt that quantitation on a simple scale of 0 to 3 would be in closer accord with the possibility of clinical psychiatric evaluation than quantitation on a more elaborate scale. If, in my opinion, a particular trait was absent, the item was graded as 0. If present in minimal degree, the trait was graded as 1; if present in moderate degree, it was graded as 2; if present in maximal degree, it was graded as 3. It is submitted that such clinical quantitation or approximation of the strength of a particular trait or factor is certainly more accurate and desirable than gross categorization of a total personality. This multidimensional system made it possible to keep in constant perspective a large number of specific judgments. It is recognized that no such schema can do justice to the subtle interplay and reciprocal participation of those features of the personality which usually present an integrate of behavior. Yet it was felt that specification was desirable, if only to test the potentialities of such a method.

The work sheet of a particular patient is presented here (table 1). It will be noted that the 60 items are arranged in two columns, of 30 each. To the right of these there are several ruled columns. In the first such column, labeled "pretraumatic rating," the estimated pretraumatic value for each specific trait was placed. The columns beyond were used for listing the valuation of each trait at specific intervals after discharge from the hospital. Thus, a running quantitative assay of the post-traumatic personality was made. This then provided data concerning what changes, if any, took place with respect to each trait in the list. Thus, for instance, it may be noted that, whereas the patient was neither gay nor euphoric in his pretraumatic state, he was extremely so (with a value of 3) two months after his discharge from the hospital and moderately so (with a value of 2) six months after discharge. Other changes may be noted.

This work sheet also included information regarding other matters, such as the patient's age, sex, dates of admission to and discharge from the hospital; the duration of unconsciousness, disorientation and amnesia, and such clinical conditions as skull fracture and blood in the cerebrospinal fluid. It also included data concerning various complicating psychosocial factors, date of return to work, a categorical personality diagnosis, an estimate of the severity of the injury to the brain and of the associated bodily injuries, if any, and an estimate of the severity of the sequelae, as limited by the list of 60 items. It also provided for information concerning the family history, the personal psychiatric history and whether there had been any disproportionate

TABLE 1.—*Sample Work Sheet for Personality Study*

Scale: 0-3	Pre-traumatic Rating of Each Trait	Post-Traumatic Ratings: 1½ Mo. (Date 9/14)	3 Mo. (Date 11/30)	6 Mo. (Date 3/2)	9 Mo. (Date 5/19)
Work					
Unsteady	1	..	..	..	..
Steady, few jobs	0	..	..	..	..
Steady, many jobs	2	..	..	..	..
Alcoholism					
Time of injury	1	..	..	..	..
Chronic	2	..	..	..	..
Periodic	2	..	..	..	..
Asocial tendency	0	0	0	0	0
Timorousness	0	0	0	0	0
Prudence	1	1	1	1	1
Recklessness	1	1	1	1	1
Aggressiveness	0	0	0	0	0
Ambitiousness	0	0	0	0	0
Responsibility	1	1	1	1	1
Irresponsibility	1	1	1	1	1
Gaiety	0	3	3	2	2
Euphoria	0	3	3	2	2
Seriousness	2	0	0	0	1
Depressive state	0	0	0	0	0
Gregariousness	1	2	2	2	2
Seclusiveness	2	1	1	1	1
Egocentricity	1	1	1	1	1
Introspectiveness	1	0	0	0	0
Altrocentricity	0	0	0	0	0
Extrospectiveness	1	1	1	1	1
Sensitivity	0	0	0	0	0
"Schizoid" traits	0	0	0	0	0
Restlessness	1	1	1	1	1
Tenseness	0	0	0	0	0
Irritability	0	0	0	0	0
Excitability	0	2	2	2	1

Scale: 0-3	Pre-traumatic Rating of Each Trait	Post-Traumatic Ratings: 1½ Mo. (Date 9/14)	3 Mo. (Date 11/30)	6 Mo. (Date 3/2)	9 Mo. (Date 5/19)
Emotional Status					
Stable	2	1	1	1	1
Unstable	1	2	2	2	1
Incontinent	0	0	0	0	0
Impulsiveness	1	1	1	1	1
Fatigability	0	0	0	0	0
Apathy	0	0	0	0	0
Abulia	0	0	0	0	0
Obsessive-compulsive states	0	0	0	0	0
Hypochondriasis	0	0	0	0	0
Anxiety, chronic	0	0	0	0	0
Anxiety attacks	0	0	0	0	0
Anxiety re head	0	0	0	0	0
Anxiety re family	0	0	0	0	0
Anxiety re occupation	0	0	0	0	0
Anxiety re other matters	0	0	0	0	0
Hysteria (conversion dissociation)	0	0	0	0	0
Sex disturbance	0	0	0	0	0
Insomnia	0	0	0	0	0
Fitful sleep	0	0	0	0	0
Increased need of sleep	0	0	0	0	0
Nightmares	0	0	0	0	0
Dreams (accident)	0	0	0	0	0
Difficulties in concentration and memory	0	0	0	0	0
Headache					
Steady	0	0	0	0	0
Periodic	0	0	0	0	0
Dizziness	0	0	0	0	0
Vertigo	0	0	0	0	0
Palpitation	0	0	0	0	0
Hyperhidrosis	0	0	0	0	0
Gastrointestinal disturbances	0	0	0	0	0
Complicating Factors					
Compensation	..	0	0	0	0
Reduction in work ability	..	3	2	2	1
Persistence of accidental injury	..	0	0	0	0
Marital difficulty	0	0	0	0	0
Sexual difficulties	0	0	0	0	0
Occupation	0	0	0	0	0
Economic difficulties	0	0	0	0	0
War service	0	0	0	0	0
Return to work	..	0	0	0	0

Diagnosis of present injury: Contusion of brain; fracture of skull; Korsakoff syndrome

Severity of present injury: 3

Severity of associated injury: 0

Disproportionate reactions to previous injuries: 0

Family history: Father alcoholic

Personal psychiatric history: Psychopathic personality

Occupation: Laborer

Comment: Coma, 20 hours; disorientation, 18 days; amnesia, 18 days. Bloody cerebrospinal fluid; severe injury to brain; severe sequelae (3). Categorical personality classification: "Psychopathic." Family insists euphoria represents profound change in personality.

Admitted: 7/13/1942. Discharged: 8/29/1942.

reaction to previous injuries. The reason for inclusion of all these matters in a master work sheet was to keep a multiplicity of possible factors in view in considering each case.

This work sheet reflects the data available in the detailed record of each patient. The observations which follow are the result of studies of these completed work sheets.

CORRELATIONS; CONCLUSIONS; COMMENT

SPECIFIC FACTORS

Table 2 presents the distribution of pretraumatic personality ratings (0-1-2-3) with respect to all the traits in the list exclusive of alcoholism

TABLE 2.—*Values for Pretraumatic Traits* *

Traits	Distribution of Pretraumatic Ratings			
	0	1	2	3
Asocial attitude	88	13	1	0
Timorousness	44	37	17	2
Prudence	18	24	49	11
Recklessness	51	29	19	3
Aggressiveness	18	42	39	3
Ambitiousness	11	35	45	11
Responsibility	4	18	59	21
Irresponsibility	67	19	15	1
Gaiety	12	34	53	3
Euphoria	82	19	1	0
Seriousness	12	58	29	3
Depressive state	58	15	6	0
Gregariousness	3	25	44	30
Seclusiveness	68	21	11	0
Egocentricity	18	35	40	9
Introspectiveness	65	27	7	3
Altrocentricity	17	41	41	3
Extrospectiveness	9	36	56	1
Sensitivity	42	27	24	9
"Schizoid" tendency	100	2	0	0
Restlessness	42	32	25	3
Tenseness	49	39	22	2
Irritability	60	28	13	1
Excitability	69	27	6	0
Stability	7	28	34	33
Instability	37	37	22	6
Incontinence	101	1	0	0
Impulsiveness	48	34	19	1
Fatigability	74	24	3	1
Apathy	95	6	1	0
Abulia	97	3	2	0
Obsessive-compulsive state	76	21	4	1
Hypochondriasis	85	12	3	2
Anxiety, chronic	72	19	9	2
Anxiety attacks	94	5	3	0
Anxiety re head	99	2	1	0
Anxiety re family	80	16	6	0
Anxiety re occupation	97	4	1	0
Anxiety re other matters	94	2	6	0
Hysteria (conversion dissociation)	96	3	2	1
Sex disturbance	82	7	2	1
Insomnia	92	6	3	1
Fitful sleep	94	7	1	0
Increased need of sleep	100	1	1	0
Nightmares	90	10	2	0
Dreams (accident)	101	1	0	0
Difficulties in concentration and memory	100	1	1	0
Headache				
Steady	101	1	0	0
Periodic	93	8	1	0
Dizziness	99	3	0	0
Vertigo	101	1	0	0
Palpitation	100	2	0	0
Hyperhidrosis	98	3	1	0
Gastrointestinal disturbances	100	0	2	0

* The values in 1 case were inadvertently duplicated, thus accounting for the apparent total of 102 cases; this does not materially affect the calculations.

and work items. The first column (0) gives the number of patients for whom each trait was given a 0 value. Thus, taking the "asocial" trait as an example, there were 88 patients who were rated as lacking this trait. The next column gives the number of patients (13) in whom the trait was present in a minimal (1) degree, and, the next column, the number of patients in whom this asocial trait was present in a moderate (2) degree. The last column shows that there were no patients in whom this trait was present in a maximal (3) degree. Thus, this table presents at a glance the distribution of values specific for pretraumatic traits.

Table 3 presents the shift in trait values after head injury. This table is multidimensional. It indicates what happened with respect to each trait's pretraumatic rating. It will be noted that there are four comprehensive columns, headed as follows:

Pretraumatic rating.....	0	Pretraumatic rating.....	2
Pretraumatic rating.....	1	Pretraumatic rating.....	3

Under each of these headings are listed, in three subcolumns, the number of patients who showed a "rise" or a "fall" in value or the "same" value for the trait after trauma. Thus, each master column comprises the data on what happened to the value of that specific personality trait after head injury. To illustrate, one may take the heading "pretraumatic rating 0" and note the trait "timorousness." Reference to table 2 shows that 44 patients were given a pretraumatic rating of 0; 37 were given a rating of 1 (minimal); 17 were given a rating of 2 (moderate), and 2 were given a rating of 3 (maximal). Now, in table 3, under the master heading "pretraumatic rating 0" one can see what happened to the value of the trait "timorousness" for the 44 patients who were rated in table 2 as lacking this trait. It is noted that there was a rise in value for 12 patients. While the degree of rise is not stated, it does appear that 12 patients who lacked timorousness before head injury presented this trait after the injury. It is also noted that there was no change in the pretraumatic value for 32 of the patients. Obviously, there could be no fall in value from an 0 rating. It will be noted under the second master column heading, "pretraumatic rating 1," that of the 37 patients in table 2 who were rated as having a value of 1 (minimal) for timorousness, 13 showed a rise in the value, none showed a fall in value and 24 showed the same value after injury. Under the master heading "pretraumatic rating 2," in table 3, it is noted that of the 17 patients who were graded in table 2 as having a value of 2 (moderate) for pretraumatic timorousness, 1 showed a rise in this value after head injury, 1 showed a fall and 15 had the same value. Under the master heading "pretraumatic rating 3," in table 3, one finds what happened to the value for the trait for the 2 patients noted in table 2 as having

TABLE 3.—*Changes in Values for Post-Traumatic Traits*

Traits	Pretraumatic Rating 0 — Post-Traumatic Value			Pretraumatic Rating 1 — Post-Traumatic Value			Pretraumatic Rating 2 — Post-Traumatic Value			Pretraumatic Rating 3 — Post-Traumatic Value		
	Rise	Fall	Same	Rise	Fall	Same	Rise	Fall	Same	Rise	Fall	Same
Asocial attitude	0	0	88	0	3	10	0	0	1	0	0	0
Timorousness	12	0	32	13	0	24	1	1	15	0	0	2
Prudence	1	0	17	1	0	23	1	2	46	0	0	11
Recklessness	2	0	49	0	8	21	0	4	15	0	0	3
Aggressiveness	0	0	18	0	4	38	0	7	32	0	1	2
Ambitiousness	0	0	11	0	3	32	0	9	36	0	6	5
Responsibility	1	0	3	0	0	18	0	4	55	0	5	16
Irresponsibility	1	0	66	2	1	16	0	0	15	0	1	0
Gaiety	3	0	9	1	2	31	0	15	38	0	2	1
Euphoria	3	0	79	1	8	10	0	1	0	0	0	0
Seriousness	4	0	8	11	1	46	2	2	25	0	3	0
Depressive state	8	0	50	1	0	14	3	0	3	0	0	0
Gregariousness	0	0	3	2	2	21	0	5	39	0	9	21
Seclusiveness	3	0	65	2	0	19	0	2	9	0	0	0
Egocentricity	4	0	14	7	0	28	5	0	35	0	1	8
Introspectiveness	11	0	54	3	2	22	0	0	7	0	0	3
Altrocentricity	1	0	16	0	8	33	0	9	32	0	0	3
Extrospectiveness	0	0	9	1	2	33	0	11	45	0	0	1
Sensitivity	6	0	36	1	1	25	1	1	22	0	0	9
Schizoid tendency	0	0	100	0	0	2	0	0	0	0	0	0
Restlessness	7	0	35	9	1	22	2	4	19	0	1	2
Tenseness	14	0	35	15	2	12	2	5	15	0	1	1
Irritability	16	0	44	11	0	17	3	2	8	0	0	1
Excitability	12	0	57	9	1	17	1	0	5	0	0	0
Stability	0	0	7	2	3	23	0	15	19	0	15	18
Instability	14	0	23	16	1	20	1	2	19	0	2	4
Incontinence	5	0	96	0	1	0	0	0	0	0	0	0
Impulsiveness	3	0	45	2	4	28	1	5	13	0	0	1
Fatigability	31	0	43	13	0	11	0	0	2	0	0	1
Apathy	17	0	78	0	0	6	0	0	1	0	0	0
Abulia	26	0	71	0	0	3	0	0	2	0	0	0
Obsessive-compulsive state	10	0	66	2	0	19	1	0	3	0	0	1
Hypochondriasis	11	0	74	5	1	6	2	1	0	0	0	2
Anxiety, chronic	7	0	65	4	0	15	1	2	6	0	0	2
Anxiety attacks	11	0	83	2	0	3	1	0	2	0	0	0
Anxiety re head	31	0	68	1	1	0	1	0	0	0	0	0
Anxiety re family	3	0	77	1	3	12	0	1	5	0	0	0
Anxiety re occupation	4	0	93	2	0	2	1	0	0	0	0	0
Anxiety re other matters	14	0	80	0	0	2	0	2	4	0	0	0
Hysteria (conversion dissociation)	6	0	90	0	1	2	0	0	2	0	0	1
Sexual disturbance	6	0	76	1	1	5	0	1	1	0	0	1
Insomnia	28	0	64	2	0	4	0	1	2	0	0	1
Fitful sleep	25	0	69	0	1	6	0	0	1	0	0	0
Increased need of sleep	22	0	78	0	0	1	0	0	1	0	0	0
Nightmares	13	0	77	3	4	3	0	1	1	0	0	0
Dreams (accident)	12	0	89	1	0	0	0	0	0	0	0	0
Difficulties in concentration and memory	22	0	78	0	1	0	0	1	0	0	0	0
Headache												
Steady	16	0	85	0	1	0	0	0	0	0	0	0
Periodic	45	0	48	4	1	3	0	1	0	0	0	0
Dizziness	36	0	63	0	2	1	0	0	0	0	0	0
Vertigo	16	0	85	0	1	0	0	0	0	0	0	0
Palpitation	6	0	94	1	0	1	0	0	0	0	0	0
Hyperhidrosis	2	0	96	2	0	1	0	0	1	0	0	0
Gastrointestinal disturbance	6	0	94	0	0	0	0	0	2	0	0	0

a value of 3 (maximal) for timorousness. Both appear as having the same value after head injury. Of course, under the master heading "pretraumatic rating 3," no patients will appear in the column headed "rise," because by definition none can have a value greater than 3. However, this column ("rise") was included under "pretraumatic rating 3," as was the column headed "fall" under "pretraumatic rating 0," for purposes of symmetry in making the table.

Examination of table 3 indicates that certain pretraumatic traits tended to change more than others. These traits were: timorousness, 27 patients; recklessness, 14 patients; aggressiveness, 12 patients; ambitiousness, 18 patients; gaiety, 23 patients; euphoria, 13 patients; seriousness, 23 patients; depressive state, 12 patients; gregariousness, 18 patients; egocentricity, 18 patients; introspectiveness, 16 patients, and altrocentricity, 18 patients.

Table 3 thus presents a summary of the quantitative changes in specific personality traits after head injury. While all traits showed some change, certain traits showed most prominent changes.

TABLE 4.—*Traits in Which Change Occurred After Head Injury in 10 or More Patients*

Trait	Number of Patients Who Showed Post-Traumatic Change in Value of Trait	Number of Patients with Rise in Value	Number of Patients with Fall in Value
Timorousness	27	26	1
Recklessness	14	2	12
Aggressiveness	12	0	12
Ambitiousness	18	0	18
Gaiety	23	4	19
Euphoria	13	4	9
Seriousness	23	17	6
Depressive state	12	12	0
Gregariousness	18	2	16
Egocentricity	17	16	1
Introspectiveness	16	14	2
Altrocentricity	18	1	17
Extrospectiveness	14	1	13
Sensitivity	10	8	2
Restlessness	24	18	6
Tension	39	31	8
Irritability	32	30	2
Excitability	23	22	1
Emotional stability	35	2	33
Emotional instability	36	31	5
Impulsiveness	15	6	9
Fatigability	44	44	0
Apathy	17	17	0
Abulia	26	26	0
Obsessive-compulsive state	13	13	0
Hypochondriasis	20	18	2
Anxiety, chronic	14	12	2
Anxiety attacks	14	14	0
Anxiety re head	34	33	1
Anxiety re other matters	16	14	2
Insomnia	31	30	1
Fitful sleep	26	25	1
Increased need of sleep	22	22	0
Nightmares	21	16	5
Dreams (accident)	13	13	0
Difficulties in concentration and memory	24	22	2
Headache			
Steady	17	16	1
Periodic	51	49	2
Dizziness	38	36	2
Vertigo	17	16	1

Table 4 presents certain data abstracted from table 3. Table 4 lists those traits in which there was a post-traumatic change in 10 or more patients. It indicates the number of patients in whom there was any change and also the number of patients in whom the value for the trait was increased ("rise") or decreased ("fall"). It should be noted in particular by reference to table 3 that a substantial number of patients presented certain traits after trauma which had not been present in the personality before head injury. The data on these traits are summarized in table 5.

TABLE 5.—*Traits Appearing After Head Injury for First Time*

Trait	Number of Patients in Whom Trait Appeared Post-Traumatically for First Time	Trait	Number of Patients in Whom Trait Appeared Post-Traumatically for First Time
Timorousness	12	Anxiety attacks	11
Gaiety	3	Anxiety re head	31
Euphoria	3	Anxiety re other matters	14
Seriousness	4	Hysteria	6
Depressive state	8	Sex disturbances	6
Egocentricity	4	Insomnia	28
Introspectiveness	11	Fitful sleep	25
Sensitivity	6	Increased need of sleep	22
Restlessness	7	Nightmares	13
Tenseness	14	Dreams	12
Irritability	10	Difficulties in concentration and memory	22
Excitability	12	Headache	
Emotional instability	14	Steady	16
Emotional incontinence	5	Periodic	45
Fatigability	31	Dizziness	36
Apathy	17	Vertigo	16
Abulia	26	Palpitation	6
Obsessive-compulsive state	10	Gastrointestinal disturbance	6
Hypochondriasis	11		
Anxiety, chronic	7		

The changes in personality trait values following head injury are in accord with general clinical experience. The fact that in so many instances the trait was manifest in appreciable degree for the first time (table 5) refutes the oft expressed view that post-traumatic psychiatric symptoms represent a pretraumatic psychiatric liability to such symptoms. This view has been expressed particularly with regard to those patients who presented characteristic psychoneurotic symptoms after head injury.[4] In the present series, it may be noted that a number of patients without evidence of pretraumatic existence of specific psychoneurotic traits manifested such traits post-traumatically. Thus, 10 patients showed obsessive-compulsive symptoms, 11 hypochrondriacal symptoms, 6 hysterical symptoms,

4. Lewis, A., in Discussion on Differential Diagnosis and Treatment of Post-contusional States, Proc. Roy. Soc. Med. **35**:607-614, 1942.

11 clearcut symptoms of anxiety and 31 marked fatigability (neurasthenia), for the first time after injury. It appears, therefore, that the development of psychoneurotic symptoms in patients with head injury does not justify an assumption that such patients had pretraumatic neurotic personalities.

Reference to table 4 shows that the number of patients for whom changes in the trait value followed head injury paralleled the number of those who first manifested the trait after head injury. In table 6 the traits are presented in the order of frequency of involvement (change).

TABLE 6.—*Traits in Order of Frequency of Occurrence After Head Injury*

Trait	Total Number	Number of Patients with Post-Traumatic Change in Value for Trait	
		Number with Rise in Value	Number with Fall in Value
Periodic headache	51	49	2
Fatigability	44	44	0
Tension	39	31	8
Dizziness	38	36	2
Emotional instability	36	31	5
Emotional stability	35	2	33
Anxiety re head	34	33	1
Irritability	32	30	2
Insomnia	31	30	1
Timorousness	27	26	1
Abulia	26	26	0
Fitful sleep	26	25	1
Restlessness	24	18	6
Difficulties in concentration and memory	24	22	2
Seriousness	23	17	6
Gaiety	23	4	19
Excitability	23	22	1
Increased sleep need	22	22	0
Nightmares	21	16	5
Hypochondriasis	20	18	2

The time of appearance of these changes in trait values after head injury varied considerably. In most cases the symptoms (other than headache and dizziness) began to appear shortly after the patient's discharge from the hospital and developed slowly to a maximum in from three to six weeks after discharge. A few patients showed a longer latent period and did not present symptoms until several months after discharge. It may be stated here that these few patients had complicating psychosocial factors in their lives which in their intensity and chronologic appearance tended to parallel the development of symptoms. The appearance of acute neurotic symptoms during hospitalization was infrequent and usually indicated a later intensification and persistence of such symptoms.

The duration of these post-traumatic symptoms also varied. Most had reached their peak at six weeks and were substantially receding at three months. However, approximately 50 per cent of the patients showed some persistence of symptoms at six months, and approxi-

mately 15 per cent of the patients had symptoms which persisted a year or longer. One patient who suffered contusion of the brain and a brief period of unconsciousness, with a gross residual cosmetic defect of his forehead, showed irritability two years after head injury.

The duration of incapacity for work paralleled the persistence of symptoms, although most patients returned to work before they were entirely free of symptoms.

PERSONALITY CATEGORIES

In order to test popular conceptions concerning the relationship between categorical personality classifications, such as pretraumatic, normal, psychoneurotic, psychovariant and psychopathic personalities, as well as to test my previous conclusions about such categories, each patient in this study was classified under one of the following four headings, each of which has been previously defined as follows:[1]

Normal Personality.—A person who is in harmony with himself and his environment, is virtually free of psychoneurotic traits and other personality imbalances, is not habitually in conflict with the ethical and social standards of society, is free of addiction to alcohol, maintains satisfactory personal, social and occupational adjustments and presents a general integration of objectives and behavior. This does not exclude the possible existence of some personality bias, such as egocentricity or timidity, or even a history of brief transient neurotic symptoms.

Psychopathic Personality.—A person who has shown extreme failure in social and intrapersonal adaptation, associated with impulsiveness, defective self control, lack of fixity of purpose, instability of effort and undependability in his work. In this category are wide variations. There may or may not be associated psychoneurotic phenomena. It is possible to make an unlimited series of subtypes of the psychopathic personality. I have selected seven: inferior, alcoholic, affective, aggressive, criminal, schizoid and miscellaneous types. As these subtypes are not discussed in the present study, they are not defined here.

Neurotic Personality.—A person whose behavior and experience are substantially affected by the existence of traits or symptoms which characterize the generally accepted psychoneurotic syndromes of neurasthenia, hypochondriasis, anxiety neurosis, obsessional neurosis and hysteria.

Personality Variant.—A person who, while not psychotic, frankly psychoneurotic or psychopathic, has appreciably more weighting of the personality than the average normal subject. Such patients represent deviations from the average. The personality bias includes such traits as timidity, egocentricity, irritability, cantankerousness, hypersensitivity, moodiness, emotional lability, solemnity or general light heartedness.

The distribution of categorical personality diagnoses was as follows: Fifty-one patients were classified as normal, 13 as psychoneurotic, 14 as psychopathic and 23 as psychovariant personalities.

Table 7 presents the values for a list of traits on which the diagnoses of "psychopathic personality" were based. It may be noted that alcoholism was present in 11 of these patients, although in 1 it was relatively

mild. Patient B. had many psychoneurotic symptoms, as well as addiction to alcohol; but his gross character defects led to his classification as a "psychopathic personality." Only 2 patients were delinquent. One of these was a young man who could not refrain from following his impulses to drive other persons' automobiles. In 3 of the patients (S., J. and C.) alcoholism of varying degree was coupled with sensitiveness, restlessness and tenseness. Seven of these patients had a poor work record; 5 had associated alcoholism. Eight exhibited recklessness; 5, aggressiveness; 10, irresponsibility; 7, egocentricity, and 7 impulsiveness.

The "psychoneurotic" patients all had good work records and were free of alcoholism. Whereas the average value for "sensitiveness" in

TABLE 7.—*Special Trait Values for Pretraumatic Psychopathic Personalities* *

Patient	Alcoholism	Unsteady Work Habits	Asocial Traits	Recklessness	Aggressiveness	Irresponsibility	Egocentricity	Emotional Instability	Impulsiveness
V.	0	2	2	2	2	2	2	3	2
Mc.	3	2	1	2	0	2	0	0	2
P.	0	2	0	2	3	2	3	2	3
K.	2	0	0	2	1	2	0	0	2
G.	2	1	0	2	1	2	2	1	1
C.	2	1	0	1	0	1	1	1	1
F.	2	0	0	2	2	2	2	2	2
W.	3	2	0	1	1	2	1	1	2
F.	3	2	0	0	2	0	1	1	0
K.	3	3	0	0	0	2	1	1	1
S.	3	0	0	2	1	1	1	1	0
J.	2	1	0	0	0	1	3	0	0
C.	1	1	0	2	2	2	2	3	2
B.	3	2	0	1	1	3	2	2	0

* Rated on a scale of 0 to 3.

"psychopathic personalities" was less than 1 (on the scale of 0 to 3), the average value for this trait in the "psychoneurotic subjects" was in excess of 2.

The "normal" subjects also had good work records and were essentially free of alcoholism. None had a value greater than 1 for any of the recognized psychoneurotic traits (fatigability, hypochondriasis, anxiety states, obsessive-compulsive states and hysteria). In general they were emotionally stable. There were no evidences of restlessness, tenseness, irritability or excitability. The traits of prudence and timorousness were much higher in these patients than in the psychopathic personalities in whom they were virtually absent. The greatest differences between individuals in this group of normal personalities was in regard to the traits of gregariousness, ambitiousness, extrospection, gaiety and seriousness.

Chart 1 presents the comparative average values (on a scale of 0 to 3) for each of the 60 personality items for the four pretraumatic

Chart 1.—Comparison of average values for each of 60 personality characteristics of patients with pretraumatic psychoneurotic, psychopathic, psychovariant and normal personalities.

categories (normal, psychovariant, psychopathic, psychoneurotic). The key is given on the chart. The data are thus presented on which the categorical distinctions are based.

Chart 2 presents a comparison of the pretraumatic and post-traumatic average values for each of the 60 personality characteristics of those patients who were classified as having a pretraumatic normal personality. Charts 3, 4, and 5 present similar data on the patients with pretraumatic psychoneurotic, psychovariant and psychopathic personalities.

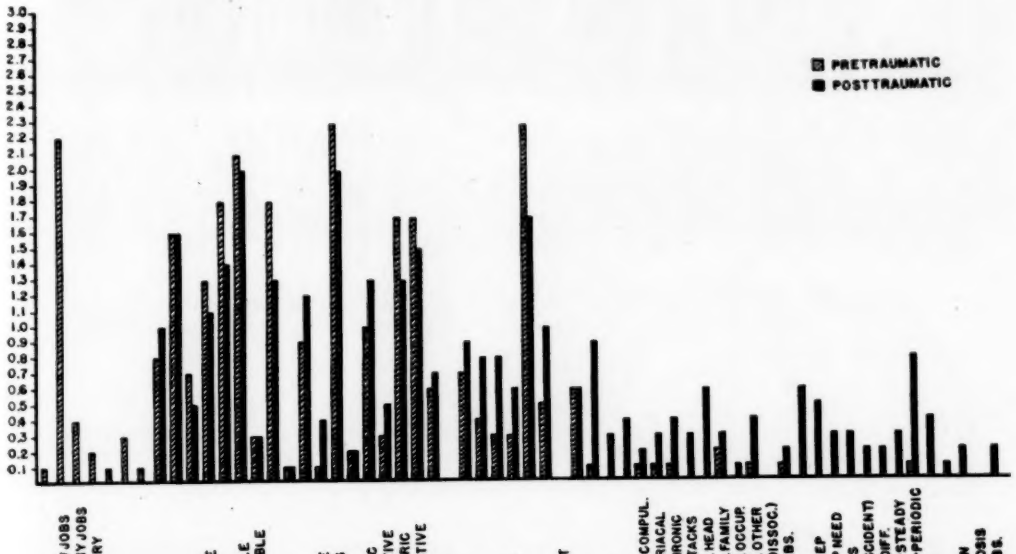

Chart 2.—Comparison of the pretraumatic and post-traumatic average values for each of 60 personality characteristics of patients with pretraumatic normal personality.

In this chart, and in charts 3, 4 and 5, pretraumatic values are represented by hatched rectangles; post-traumatic values, by solid rectangles.

Chart 6 is derived from charts 2 to 5. It presents those traits in which there was a change of 10 per cent or more between the pretraumatic and the post-traumatic average value for any 4 personality categories. It will be noted that the pretraumatic normal personalities showed such a change in respect to 26 items. The average for the change of values for pretraumatic normal personalities was approximately 14 per cent. The psychovariant personalities showed a change in respect to 19 items and an average change of 13 per cent. The psychopathic personalities showed a change in respect to 6 items, with an average change of 12.5 per cent. The

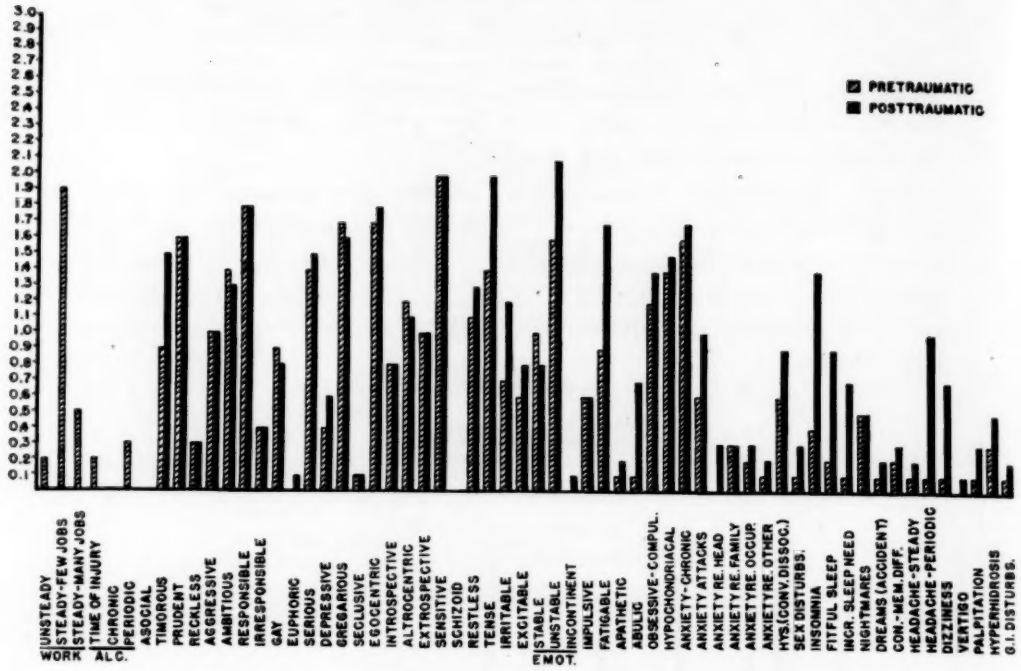

Chart 3.—Comparison of the pretraumatic and post-traumatic average values for each of 60 personality characteristics of patients with pretraumatic psychoneurotic personality.

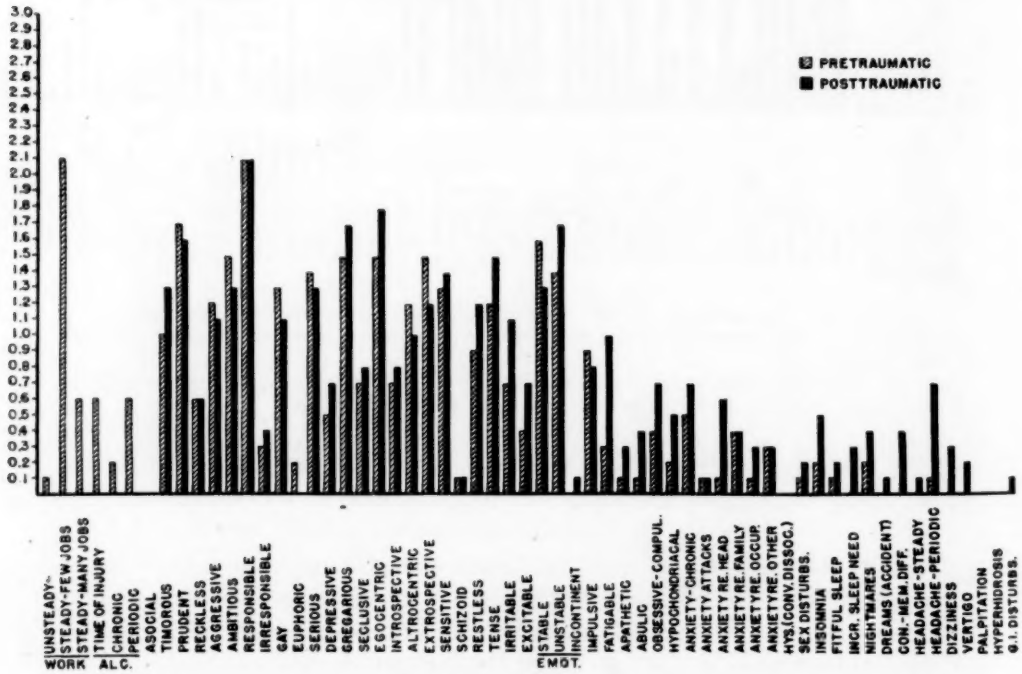

Chart 4.—Comparison of the pretraumatic and post-traumatic average values for each of 60 personality characteristics of patients with pretraumatic psychovariant personality.

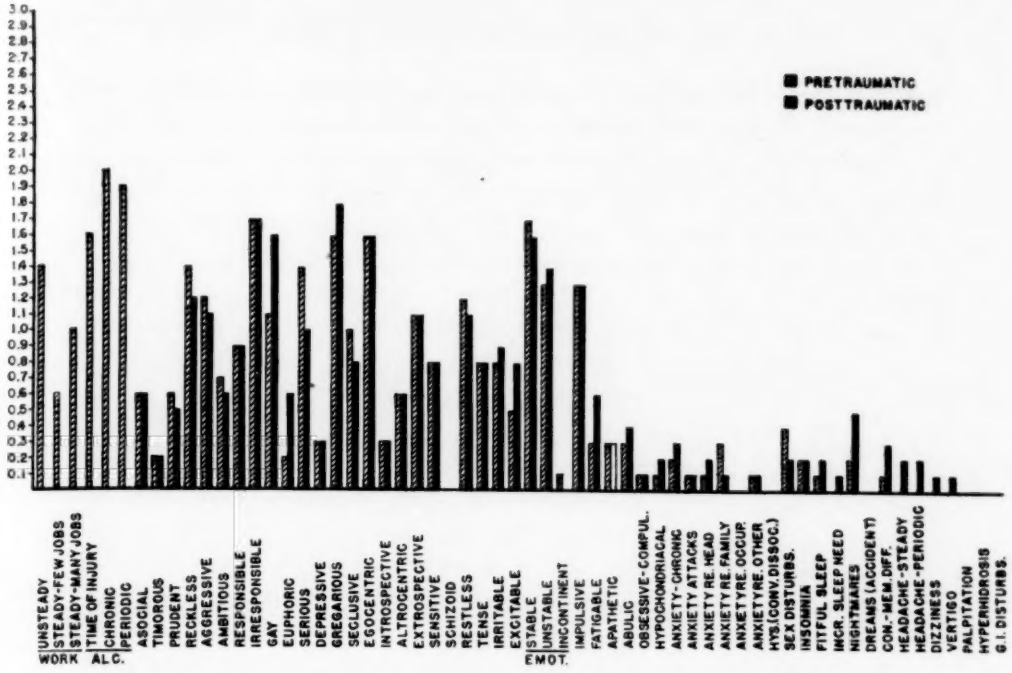

Chart 5.—Comparison of the pretraumatic and post-traumatic average values for each of 60 personality characteristics of patients with pretraumatic psychopathic personality.

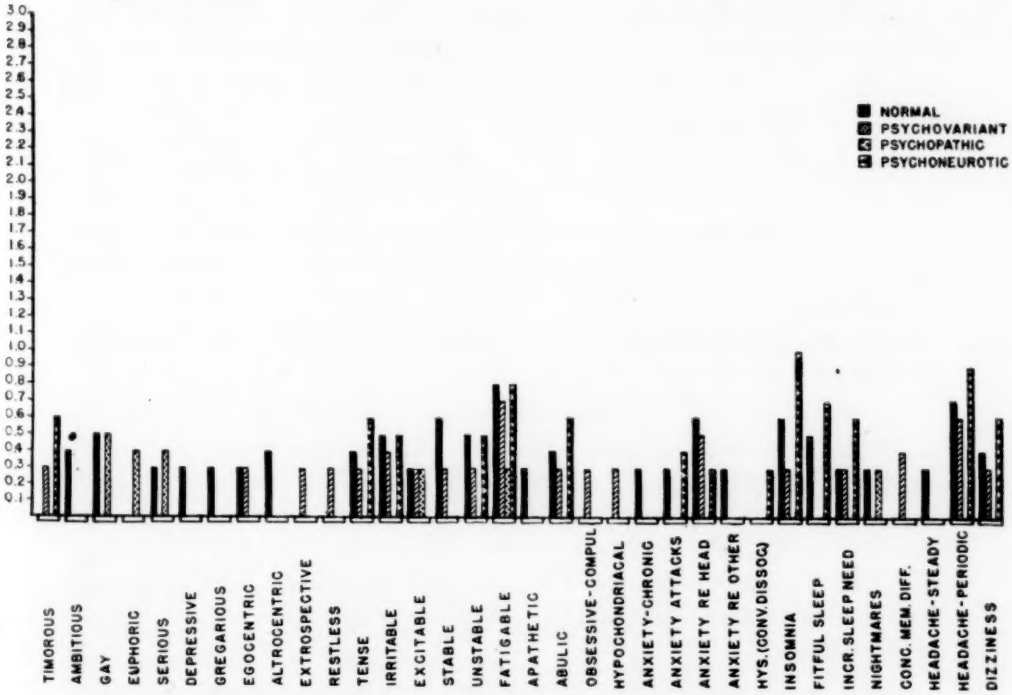

Chart 6.—Comparison of those traits in which significant differences (10 per cent or more) were found between the pretraumatic and the post-traumatic average values for patients with pretraumatic psychoneurotic, psychopathic, psychovariant and normal personalities.

psychoneurotic personalities showed a change in respect to 14 items, with an average change of 20 per cent. It should be kept in mind that these psychoneurotic personalities had such high pretraumatic values for the special traits which led to the categorical diagnosis that there was little, or no, room left for change in value. The average change of value for the combined psychoneurotic, psychovariant and psychopathic personality groups was 13 per cent. When this is compared with the average change of value of 20 per cent for the psychoneurotic personalities, it appears that there was approximately a 50 per cent greater change for the psychoneurotic personalities than the average change for the other three categories.

In the psychoneurotic group the greatest changes took place with respect to fatigability, disturbances in sleep, headache and dizziness. It would appear, then, that pretraumatic psychoneurotic personalities may have a greater liability to the development of such post-traumatic symptoms. However, it will be noted that the "normal personalities" run a close second with respect to most of the changes and equal the psychoneurotic personalities with regard to changes in values for fatigue and exceed them with respect to other items.

When attention is directed to the generally recognized neurotic traits, the following correlations appear. The only trait which was substantially affected in all four personality groups was that of fatigability. The average change of values (on a scale of 0 to 3) in each of these groups was as follows:

Normal	0.8	Psychovariant	0.7
Psychoneurotic	0.8	Psychopathic	0.3

Only the psychovariant personality group showed appreciable changes (0.3) with respect to obsessive-compulsive and hypochondriacal symptoms.

The changes in respect to the categories of anxiety are presented in table 8.

It appears, then, that psychoneurotic personalities were slightly more liable to development of anxiety attacks than were other personality types, although the figure for the normal personalities suggests an even greater propensity in such persons because that group was entirely free of anxiety attacks before head injury. It is to be noted, also, that anxiety concerning the head was greater among the normal and psychovariant personalities than among the psychoneurotic personalities.

The psychopathic personalities showed the greatest changes in respect to an increase in or development of gaiety and/or euphoria and a decrease in seriousness. This cannot be considered a basis for generalization, as the particular patients who showed these changes not

only had suffered surgically severe head injury (fractured skull, contused or lacerated brain, intracranial hematoma) but also had histories of substantial chronic alcoholism. It is my impression that the preceding chronic alcoholism played a large part in contributing to the reactions of gaiety and euphoria, for such were not seen to an appreciable degree in patients in other personality categories who had suffered equally severe surgical head injury. It should be added that it was the same few psychopathic personalities with post-traumatic euphoria who were suspected of having post-traumatic dementia. Denny-Brown [2] noted that the elimination of patients over 55 years of age who had chronic alcoholism eliminated cases of post-traumatic dementia. He noted, further, by reference to the case of a normal, intelligent youth who had suffered gross laceration of both frontal lobes with a buzz saw, that the absence of a post-traumatic dementia in that case threw "doubt on the ability of trauma alone to induce persistent dementia in a healthy brain." By the same token, it is

TABLE 8.—*Correlations of Personality Categories with Average Change in Values for Types of Anxiety*

Type of Anxiety *	Personality Category			
	Normal	Psycho-neurotic	Psycho-variant	Psycho-pathic
Chronic	0.3	0	0	0
Attacks	0.3	0.4	0	0
Re head	0.5	0.3	0.4	0
Re other matters	0.3	0	0	0

* The trait values are rated on scale of 0 to 3.

probable that severe injury to a healthy brain will not in itself result in post-traumatic euphoria. However, this entire field is subject to contributions which may be offered by the recent work in surgical lobotomy. The euphoria which appeared in the patients with psychopathic personalities in this series who had received gross injuries may, on the other hand, have been expressive of an underlying irresponsibility and obliviousness to the patient's own welfare, factors which are apparent in most psychopathic personalities.

It appears, then, that patients with the pretraumatic psychoneurotic personality may not exhibit a striking aggravation of neurotic symptoms after head injury but will in general show a greater post-traumatic reaction than those in the other groups. This conclusion is supported by the data in table 9, which presents correlations between pretraumatic personality characteristics and clinical approximations of the severity of the psychiatric sequelae of the head injury (on a scale of 0 to 3). It appears that the occurrence of sequelae is most probable in psychoneurotic personalities, next most probable in psycho-

variant personalities, less probable in normal persons and least probable in psychopathic personalities.

SEVERITY OF HEAD INJURY

It has been pointed out by Denny-Brown [2] that the assessment of the severity of a head injury requires inclusion not only of the immediate post-traumatic surgical, as well as the behavioral, state but also various complicating psychologic factors. Of the patients in the present study, 21 exhibited prolonged disorientation, ranging from five hours to over a week. Of this group there were 3 patients who had bloody cerebrospinal fluid, fractured skull or intracranial hematoma and who had been subjected to craniotomy and associated neurosurgical treatment. Two of these patients presented maximal post-traumatic mental

TABLE 9.—*Estimated Severity of Sequelae of Head Injury Correlated with Pretraumatic Personality Type*

Personality Type *	Total No. of Patients	Severity of Sequelae to Head Injury: 0 No. of Patients	0 Per Cent of Total	1 No. of Patients	1 Per Cent of Total	2 No. of Patients	2 Per Cent of Total	3 No. of Patients	3 Per Cent of Total	Total No. of Patients with Sequelae of Any Degree	Per Cent of Original Group with Sequelae
Normal.....	51	26	51	9	18	9	18	7	14	24	48
Psychopathic.....	14	8	57	2	14	1	7	3	21	6	42
Psychovariant....	23	9	39	6	26	4	17	4	17	14	60
Psychoneurotic...	13	5	39	2	15	1	8	5	39	8	39

* Rated on scale of 0 to 3.

symptoms. Both had been rated as pretraumatic psychopathic personalities. One of these patients underwent a gross personality change. Previous to his head injury he had been seclusive and secretive, was substantially alcoholic but had a fair work record and was moderately responsible in his obligations to his work and family. After his head injury he became expansive, circumstantial, euphoric and emotionally unstable. He confided freely in his family and had no insight concerning his changed personality. He had difficulty with his concentration and memory. This was at its worst in the first two months after head injury, and, although there was gradual improvement, there was some persistent intellectual defect, even at nine months. It is of interest to note that he had no post-traumatic neurotic symptoms of any sort and no dizziness or headache. This man was 43 years of age. He worked as a laborer. His non-neurotic change in personality suggests, as previously noted, an organic cause, probably the result of trauma superimposed on a brain which had already been made vulnerable by chronic alcoholism. Although there was some litigation pending in this case, it did not seem to have any influence

on the symptoms. The patient was too oblivious to most things to be particularly concerned with such an issue.

The second of this group of severely injured patients, aged 32, was an irresponsible male laborer with a history of pretraumatic alcoholism, gross irresponsibility, emotional instability and multiple neurotic symptoms. After his head injury he manifested: an increase in fatigability; a decided exacerbation in the frequency and severity of anxiety attacks (present minimally before injury); increased hypochondriasis; preoccupation concerning the state of his heart and lungs; intense anxiety concerning his head; nightmares; difficulties in concentration and memory; headaches, both steady and periodic; dizziness, and vertigo. On the other hand, he showed an increase in emotional stability (except for his acute neurotic symptoms) and became less irritable and somewhat more responsible. He exhibited an increase in gaiety, which may be compared with the euphoria of the previous patient. Prior to his injury he was having difficulties in his marriage and work. His electroencephalogram remained abnormal for several months but cleared completely in four months. In such a case it is impossible to select one factor as the sole cause of the sequelae. The development of a state of gaiety disproportionate to the situation suggests persistent damage to the brain. Or, again, it may be a summation of the effect of severe trauma on the brain of a chronic alcohol addict. It is of interest to note the parallel development of both neurotic symptoms and increased emotional stability.

The third patient was a 20 year old man. In addition to a compound fracture of the skull and an extradural hematoma, he had sustained a fracture of his left clavicle and humerus, with palsy of the radial nerve and ankylosis. He had been categorically rated as a pretraumatic "normal" personality. He had a good work history and was guileless, responsible, serious, gregarious, altrocentric, rather sensitive and irritable and free of neurotic traits. He presented no psychiatric sequelae to the head injury, not even a headache. Previous to his head injury he had been subject to occasional dizziness, but he suffered no increase in this disturbance. He returned to work five months after his head injury, although his arm was not yet healed. Why did he not exhibit psychiatric sequelae? The answer is not clear. As there was no persistent intellectual impairment after head injury and no euphoria or gaiety, I am not inclined to postulate persistent damage to the brain, which might have made him oblivious to his state. The brain of a nonalcoholic youth of 20 is probably less vulnerable than that of a chronic alcohol addict of an older age group. The severe injury to the arm would have justified a substantial state of anxiety; yet he showed virtually none—not even concerning the arm itself. In a search for a possible explanation inquiry was

made concerning constitutional factors. He had long been at odds with his family because of their general irresponsibility and obliviousness to the responsibilities of everyday life. Both parents were happy-go-lucky and improvident. Could an injury to the brain have mobilized such latent tendencies in him? Certainly, there is no evidence to support such a speculation, nor can one invoke the categorical pretraumatic diagnosis of "normal," because a scrutiny of the details of his personality shows that in the "normal" group he was one of the most serious and might thus have been expected to react with greater gravity to a difficulty. This case illustrates the difficulty, or impossibility, of relating psychiatric sequelae to the surgical severity of an injury to the brain.

In addition to these 3 patients, there were 9 who were considered to have suffered very severe acute injury to the brain, as judged by prolonged coma, disorientation and amnesia, with grossly bloody cerebrospinal fluid in each case, coupled with fracture of the skull in 6. Three patients had been subjected to craniotomy for débridement of compound, comminuted fractures. The average severity of psychologic sequelae (including headache, dizziness and work disability), on a scale of 0 to 3, was 1.3. The categorical pretraumatic diagnoses of these 9 patients were as follows: psychopathic personality, 1 patient; psychovariant personality, 3 patients; normal personality, 5 patients, and neurotic personality, none.

Nineteen patients were classified as having suffered moderately acute injury to the brain. They had all manifested substantial disturbances of consciousness, orientation and memory; in addition, 14 had grossly bloody cerebrospinal fluid. Eleven had skull fractures. The average severity of psychologic sequelae in this group was 1.3, a figure identical with that for the more severely injured group.

Minimal acute injury to the brain was sustained by 70 patients. The average severity of sequelae in this group was 0.8. This figure is definitely less than that for the preceding group. It may be argued, therefore, that there is some increased statistical probability of psychologic sequelae of patients with the grosser acute head injuries. This does not prove that the psychiatric symptoms are the direct result of injury to the brain as such. When there has been compound fracture of the skull or other gross surgical injuries, the necessarily prolonged stay in the hospital might well have an impressive psychologic effect on the patient.

Table 10 tests the possibilities by a correlation of the severity of injury to the brain and the severity of sequelae. From the table it is apparent that there is not a rigid relationship between the severity of the cerebral injury and the severity of sequelae except for the

psychopathic personalities. In this group it will be noted that each of the 3 patients with severe sequelae had suffered severe injury to the brain. Euphoria developed in 2, with evidences or suggestions of dementia. The changes in these patients have already been described, as was the state of the patient with severe damage to the brain, who had only minimal sequelae. In the group with "normal" pretraumatic personalities, there were 7 patients with severe injury to the brain; of these, 3 had no sequelae, 1 minimal sequelae, 1 moderate sequelae and 2 maximal sequelae. In the same group it should be noted that 4 of the 7 patients who exhibited maximal sequelae had sustained only

TABLE 10.—*Estimated Severity of Injury to Brain Correlated with Estimated Severity of Sequelae in Various Personality Categories*

Personality Type	Severity of Sequelae *	Severity of Brain Injury † 1	2	3
		Number of Patients		
Normal	0	20	4	3
	1	4	4	1
	2	6	2	1
	3	4	1	2
Psychoneurotic	0	5	0	0
	1	2	0	0
	2	0	1	0
	3	5	1	0
Psychopathic	0	7	1	0
	1	1	0	1
	2	1	0	0
	3	0	0	3
Psychovariant	0	6	1	2
	1	3	3	0
	2	3	0	1
	3	1	3	0

* Rated on scale of 0 to 3.
† Rated on scale of 1 to 3.

minimal injury to the brain. None of the patients with pretraumatic psychoneurotic personalities sustained severe injuries to the brain, and only 2 sustained moderate cerebral injuries. Yet it should be noted that the psychoneurotic patients did show a larger portion of sequelae than either of the other groups. In the group of 3 patients with psychovariant personalities who sustained severe injuries to the brain, only 1 had even moderate sequelae, while 2 had no sequelae. It appears, thus, from table 10 that, except for the psychopathic personalities, there is little correlation between the severity of the injury to the brain and the sequelae of such injury.

COMPLICATING FACTORS

When a person sustains a head injury, he may in addition, and often does, suffer injury to other parts of his body. The persistence of such associated injury contributes to a continuance of the patient's interest in himself. This may be particularly so if such associated

injury prevents a return to work. On the other hand, the persistence of an associated injury or injuries appears in some cases to act as a distraction. In every case of head injury, then, one must take into account the possible effect of an associated injury, if such occurred. In general there was a high correlation of persistence of associated bodily injuries, prolonged work disability and persistence of psychiatric symptoms.

One must not lose sight of the fact that a head injury always involves a person as such rather than an arbitrarily defined part of that person. Such a person can be understood only in the light of his constitution and conditioning experiences. His reaction to a head injury, as to any incident in his life, is affected by what he was previous to that incident. In the present studies notice was taken of the possible existence of the following complicating psychosocial factors:

Marital or domestic difficulties
Sexual maladjustments
Occupational stresses and hazards
Financial difficulties
Impending induction into the armed forces

Under existing social legislation, provision is usually made for compensation to those injured in the course of their occupations. In addition, the law requiring that motor vehicles carry insurance to provide compensation in cases of bodily injury makes the frequency of litigation high. It was noted, therefore, with respect to each case whether there was any issue of compensation or litigation.

Table 11 presents an analysis of the data on all patients in this study who had sequelae of the head injury. In this table, the personality type, the severity of the sequelae and the severity of the injury to the brain are presented, together with data concerning any associated injury, the existence of compensation or litigation problems, other complicating factors and the time of return to work.

From a study of this table, it is obvious that there was a high correlation between the existence of pending litigation, continuing work disability and persistent psychiatric symptoms (sequelae). In general, this is greatly out of proportion to the estimated severity of the cerebral injury as such. The interpretation of this phenomenon is open. It would appear that the existence of litigation at the very least tends to maintain the patient's focus on the subject, particularly as legal processes are extended. However, contrary to some judgment, the termination of litigation does not generally terminate the symptoms promptly. It undoubtedly does have a salutary effect on the symptoms to the degree that one factor which has tended to keep the patient's mind on himself has been eradicated. In no case in this series was

TABLE 11.—*Analysis of Data on Patients with Sequelae to Head Injuries*

Personality	Severity (Scale 0-3) Sequelae	Brain Injury	Associated Injury	Compensation Litigation	Other Complicating Factors	Return to Work
Psychopathic.....	1	1	—	..	..	Prompt
	1	3	—	..	Dementia (?)	2 mo.
	2	1	—	+	Marital trouble	1 mo.
	3	3	—	—	..	1 yr.++
	3	3	—	+	..	1 yr.+
	3	3	—	+	Abnormal electrocardiograph—4 mo.	9 mo.
Psychovariant...	1	1	—	—	..	1 mo.
	1	1	—	—	Marital trouble	1 wk.
	1	1	—	—	Persistent headache	3 mo.
	1	2	Compound fracture of both legs	—	Dizziness—12 mo.	1 yr.
	1	2	—	—	..	2 mo.
	1	2	Torn tibial tubercle	+	..	Over 6 mo.
	2	1	—	+	Financial difficulties	Over 6 mo.
	1	2	—	—	Domestic difficulties	Over 6 mo.
	2	1	—	—	..	1 mo.
	2	3	Paralysis of 6th and 7th nerves	—	..	Over 6 mo.
	3	1	Synovitis (knee)	+	Marital trouble	3 mo.
	3	2	Ulcers and abrasion of leg	+ +	Occupational hazards —fire captain	6 mo.
	3	2	Amputation—toes and foot	+	Occupational hazards	Over 7 mo.
	3	2	—	+	Sexual and financial difficulties	4 mo.
Psychoneurotic...	3	2	Fracture of zygoma	+	—	3 mo.
	3	1	Burns	+	Occupational hazards —fireman	6 mo.+
	3	1	Laceration of face; deafness (8th nerve)	+	—	3 mo.
	3	1	Marked dizziness	+	—	1 mo.
	3	1	—	+	Marital trouble	3 wk.
	2	2	Sprain of back	+	—	2 mo.
	1	1	—	—	Financial	3 mo.
	1	1	Fractured nose	—	—	1 mo.
Normal.....	3	3	Depression of skull above eye	+	Cosmetic defect	2 mo.
	3	3	Squint; sprained wrist	+	Persistent squint, etc.	1 yr.
	3	1	Multiple lacerations	+	Occupational hazards —fireman	9 mo.
	3	1	—	+	Illegitimate pregnancy, etc.	3 mo.
	3	1	Tinnitus	+	—	7 mo.+
	3	1	—	+	Fireman—recovery on change of jobs	3 mo.
	3	2	Fractured ribs, 7th nerve	+	—	6 mo.+
	2	3	—	—	Impending induction	3 mo.
	2	1	Lacerated scalp	+	Marital trouble	2 mo.
	2	1	Infection of leg with sinus traits	+	Marital and financial trouble	2 mo.
	2	1	—	+	Sexual difficulty	3 mo.
	2	1	Back sprain	+	—	3 mo.
	2	1	—	+	Occupational hazards —fireman	4 mo.
	2	1	Back sprain, scar over eye	+	—	3 mo.
	2	2	Abrasions	+	—	3 mo.
	2	2	—	+	—	2 wk.
	1	1	—	—	Impending induction	3 mo.
	1	1	—	+	Occupational—policeman	4 mo.
	1	..	—	—	—	1 mo.
	1	..	—	—	—	1 mo.
	1	1	—	—	—	1 mo.
	1	1	—	—	3 sons in military service	1 mo.
	1	2	—	+	—	1 mo.
	1	2	Fractured ribs	—	Diabetes, thyroid, etc.	4 mo.
	1	2	Paralysis, 5th and 6th nerves	—	Marital trouble	3 mo.
	1	2	—	+	—	1 mo.
	1	3	Epilepsy and cosmetic defect	—	—	1 mo.

a diagnosis of malingering made or suspected. It should be added, as has been stated before, that most patients returned to work long before litigation was terminated.

When compensation was being paid to an injured person on the basis of industrial accident insurance, the convalescence was usually much longer. This was particularly noticeable in cases of persons with hazardous occupations, such as firemen and police officers.

In order to test the distributional relationships involving litigation to see whether there was any particular incidence or weighting, a scattergram (table 12) was devised in which various combinations

TABLE 12.—*Scattergram, Showing Number of Patients with Various Combinations of Factors* *

	N	O	P	Q		N	O	P	Q
ACGIK	0	1	1	1	BCGIK	..	..	..	1
ACGIL	..	..	..	..	BCGIL	..	..	..	..
ACGIM	..	..	..	..	BCGIM	..	..	1	..
ACGJK	1	..	..	..	BCGJK	1	1	..	..
ACGJL	..	..	1	..	BCGJL	..	..	..	..
ACGJM	..	..	1	..	BCGJM	..	..	..	..
ACHIK	..	1	..	..	BCHIK	2	1	..	..
ACHIL	..	..	..	..	BCHIL	..	1	1	..
ACHIM	..	1	..	..	BCHIM	..	..	..	1
ACHJK	5	..	..	..	BCHJK	7	..	1	..
ACHJL	1	..	3	1	BCHJL	1	1	1	..
ACHJM	..	..	..	..	BCHJM	..	..	1	..
ADGIK	..	..	..	..	BDGIK	2	..	..	..
ADGIL	..	..	..	..	BDGIL	..	..	..	1
ADGIM	..	..	1	..	BDGIM	..	..	1	1
ADGJK	..	..	..	..	BDGJK	2	1	1	1
ADGJL	..	..	..	..	BDGJL	1	1	..	..
ADGJM	..	..	..	..	BDGJM	..	..	..	1
ADHIK	1	2	..	1	BDHIK	1	1	..	2
ADHIL	..	1	..	2	BDHIL	..	3	1	1
ADHIM	..	..	..	..	BDHIM	..	..	2	..
ADHJK	4	..	..	..	BDHJK	12	2	4	1
ADHJL	..	1	..	..	BDHJL	..	4	..	..
ADHJM	..	..	..	..	BDHJM	..	1	..	..

* A, indicates litigation; B, no litigation; C, problems; D, no problems; G, chronic alcoholism; H, no alcoholism; I, associated trauma J, concussion only; K, coma of less than thirty minutes' duration; L, coma of less than ninety minutes' duration; M, coma of more than ninety minutes' duration; N, disorientation of less than one hour; O, disorientation of less than three hours; P, disorientation of less than twenty-four hours, and Q, disorientation of more than twenty-four hours.

were correlated against four degrees of disorientation. In all, 31 patients were engaged in litigation and 70 patients were not. In the left half of the scattergram litigation is the one common factor for the 31 patients dealt with there; in the right half of the scattergram the absence of litigation is the one common factor. The other factors considered are existence of other complicating psychosocial factors; nonexistence of psychosocial factors; existence of chronic alcoholism; absence of alcoholism; associated bodily injury; clinical diagnosis of simple concussion, and coma of less than thirty minutes' duration, ninety minutes' duration or more than ninety minutes' duration.

These items were given key letters, as follows: A, existence of litigation; B, absence of litigation; C, existence of complicating psycho-

social factors other than litigation; D, absence of complicating psychosocial factors other than litigation; G, chronic alcoholism (pretraumatic); H, absence of alcoholism; I, associated bodily injury; J, clinical diagnosis of concussion; K, coma of less than thirty minutes' duration; L, coma of less than ninety minutes' duration; M, coma of more than ninety minutes' duration.

Every possible combination of these items was arranged, and the number of patients with each combination was noted. These were then correlated with the duration of disorientation following the head injury. There were four categories of disorientation, arranged according to the following key letters: N, disorientation of less than one hour; O, disorientation of less than three hours but more than one hour; P, disorientation of less than twenty-four hours but more than three hours; Q, disorientation of more than twenty-four hours.

From this scattergram it appears that none of these factors other than *A* or *B* were present by chance in such large degree as materially to weight the data.

Comment.—It is apparent from the foregoing data that the psychiatric sequelae of head injury cannot be related to one particular factor. It is obvious that neither severe acute injury to the brain nor a heavily burdened personality will in itself explain the appearance and persistence of psychiatric sequelae as such. Certainly, some of the patients in this series who were heavily burdened with neurotic traits recovered from the acute head injury without sequelae. I was particularly interested not only in ascertaining if possible why patients have sequelae but also why some patients did not have sequelae. The reasons that patients did not exhibit sequelae were about as complex as the reasons that some did. On the whole, however, the patient who was altrocentric rather than egocentric, social minded and endowed with a high sense of responsibility was most likely to escape substantial sequelae despite the fact that such a person might be heavily burdened with neurotic traits.

In part I [1] it was noted that among the patients presenting posttraumatic mental symptoms there was a slight predominance of pretraumatic neurotic personalities. It was argued, however, that the statistical difference between such a group and other personality categories was insignificant. Those statements must be modified in the light of the observations which appear in the present paper, and which have been based on more intensive personality study. The group of pretraumatic psychoneurotic personalities as a whole did show a substantially greater degree of psychiatric sequelae than did other groups. However, it must be stressed that this difference is not great enough to permit any generalizations other than those applying to large series

of cases. Pretraumatic normal personalities closely approached the psychoneurotic personalities in the degree of psychiatric sequelae.

The syndromes following trauma to the head cannot be categorically related to the acute head injury as such, to the pretraumatic personality or to complicating factors. There appears to be little validity for continuing the commonly accepted term "postconcussion syndrome," because if such a term had validity there should be a relationship between severity of the concussion as measured by the duration of unconsciousness and the severity of the sequelae. No such relationship has been demonstrated. Denny-Brown [2] has presented convincing data in support of his proposal that the term "postconcussion syndrome" be dropped. In view of the fact that little evidence exists for any relationship between cerebral contusion as evidenced by bloody cerebrospinal fluid and the common sequelae of head injury, it is also proposed that such a term be dropped. Denny-Brown [2] has used the term "post-traumatic cerebral syndrome." This is more acceptable than any term previously proposed because it does not restrict consideration to any specially assumed type of injury to the brain. It is suggested, however, that the wording of that term be revised to read "post-cerebral-traumatic syndrome."

The one conclusion which emerges from this study is that generalizations cannot be applied to a particular case. In various cases there may be great differences in the causes of the sequelae. In a particular case the sequelae are likely to be the resultant of various factors rather than of a particular one.

SUMMARY

One hundred and one civilians with acute head injuries were subjected to intensive study of multiple factors in the pretraumatic and the post-traumatic personality status. A clinical quantitated estimate was made of the degree of each of these specific personality factors. With such a method a multidimensional perspective of each patient was obtained, by which it was possible to quantitate changes, if any, in personality following head injury.

In addition, all patients were given categorical classifications of the pretraumatic personality (normal, psychoneurotic, psychovariant and psychopathic).

Correlations were made with the nature and estimated severity of the acute cerebral trauma and with various potentially complicating factors, such as associated bodily injuries and various possible sources of psychologic stress (litigation, occupation and financial and marital difficulties).

It was found that in a number of patients neurotic symptoms appeared for the first time after head injury. In most patients psycho-

logic changes following head injury became most manifest shortly after discharge from the hospital and were at a maximum three to six weeks after discharge. The duration of post-traumatic symptoms varied but in general they were substantially receding at the end of three months. However, approximately 50 per cent of the patients showed some persistence of symptoms at six months, and approximately 15 per cent had symptoms which persisted a year or longer. The duration of incapacity for work paralleled the persistence of psychologic symptoms; but most patients returned to work before they were entirely free of symptoms.

Patients with pretraumatic psychoneurotic personalities showed a greater proportion of post-traumatic psychiatric symptoms than did patients in other groups. However, the patients with pretraumatic normal personalities were closer to the psychoneurotic patients than were members of other groups.

There was no close correlation between the severity of the acute injury of the brain and the severity of the sequelae.

There was high correlation between the existence of persistent complicating psychosocial factors, such as continuing compensation, pending litigation, occupational stresses and persistent associated bodily injuries, and the severity and persistence of psychiatric sequelae.

No correlations were found which would permit the ascription of psychiatric sequelae to one particular cause or group of causes. The psychiatric sequelae in an individual case were usually the resultant of various factors. The etiologic factors in the psychiatric sequelae in a particular case depended on specific factors in that case.

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EFFECTS OF DENERVATION ON FASCICULATIONS IN HUMAN MUSCLE

Relation of Fibrillations to Fasciculations

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IN A previous communication [1] evidence was presented to the effect that fasciculations in voluntary muscle have their site of origin not in the anterior horn cell but at the myoneural junction. This evidence consisted of the demonstration of continued fasciculations during pharmacologic block of the appropriate peripheral nerves or nerve roots and of the alteration of the frequency of fasciculations by drugs acting at the myoneural junction.

Subsequently, Denny-Brown [2] mentioned the disadvantages of pharmacologic block and indicated that this type of block could not be considered absolute in the physiologic sense, for the drug employed need not affect all the fibers in a given nerve to the same degree nor could the interference with transmission of sensory or voluntary motor stimuli permit one to conclude that all impulses were blocked.

For these reasons, confirmatory evidence for our previous premise regarding the site of origin of fasciculations was sought. It was thought that this could be supplied by observations on muscles denervated by section of the motor nerve supply. It was also hoped that by these studies some light might be thrown on the confusing problem of the relationship, or lack of relationship, between fasciculations and fibrillations.

METHODS

The experiments were performed on 2 patients with severe amyotrophic lateral sclerosis. Both patients were disabled to such an extent by their disease process that nerve section did not materially increase their disability. In one experiment the left axillary nerve was sectioned in a patient with severe atrophy, weakness and fasciculations of the muscles of both shoulder girdles. In the second experiment the right femoral nerve was sectioned in a bedridden patient with pronounced atrophy, weakness and fasciculations of the muscles of all four extremities. This patient was also the subject of the third experiment, in which the left femoral nerve was sectioned. All nerve sections were performed with the usual surgical

From the Department of Neurology of Jefferson Medical College.

1. Forster, F. M., and Alpers, B. J.: The Site of Origin of Fasciculations in Voluntary Muscle, Arch. Neurol. & Psychiat. **51**:264 (March) 1944.

2. Denny-Brown, D.: Personal communication to the authors.

precautions. In addition to simple sectioning, a portion of each nerve approximately 2 cm. in length was removed. The cut ends of the nerves were not sutured. All the wounds healed uneventfully.

Fasciculations were recorded electrically by means of a three channel, condenser-coupled amplifier with ink-writing oscillograph (Grass). The electrodes consisted of coaxial needle electrodes and of pairs of single needles placed at a distance of 0.5 cm. In deriving conclusions, only records from the coaxial needle electrodes were considered. Readings were taken prior to and after section of the peripheral nerves and from control muscles in other extremities, as well as from the muscles concerned in the present study. Electrode placements were through tattoo marks placed in the skin so that variation of placement might be reduced to a minimum. In each reading the number of fasciculations appearing in ten minutes was recorded. When neostigmine was given, the dose employed was 1.5 mg., and the intramuscular route was chosen. Atropine sulfate, 1.3 mg., was administered simultaneously with the neostigmine.

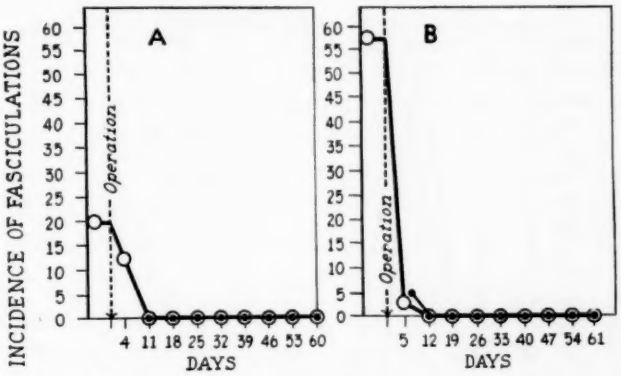

Fig. 1.—Effects of denervation on incidence of fasciculations, as observed at weekly intervals. In experiment 1 (*A*), on the fourth day after section of the axillary nerve the incidence of spontaneous fasciculations in the deltoid muscle had decreased, and on the eleventh and on all subsequent days fasciculations were absent. Neostigmine induced no fasciculations. In experiment 2 (*B*) five days after section of the femoral nerve fasciculations in the quadriceps muscle decreased and were absent on the twelfth and on subsequent days. Neostigmine was without effect after the twelfth day.

In this figure, and in figure 2, the line with large, hollow circles indicates values for spontaneous fasciculations, and the line with small, solid circles, the values for neostigmine-induced fasciculations.

RESULTS

In the control observations, in experiment 1 (fig. 1 *A*), an average of 20 fasciculations occurred in a single motor unit in the course of ten minutes. Four days after denervation the incidence was 15 fasciculations during a ten minute period. Beginning with the eleventh day, no spontaneous fasciculations appeared, nor did the administration of neostigmine produce fasciculations in the denervated deltoid muscle, despite the marked increase present in the nondenervated muscles. In experiment 2 (fig. 1 *B*) the control observations indicated an average

frequency of fasciculations of between 55 and 60 in a given motor unit during a ten minute period. Five days after denervation only 3 spontaneous fasciculations occurred, and neostigmine given intramuscularly induced only 6 fasciculations in an identical interval of time. On the twelfth day and at each succeeding seventh day reading, neither spontaneous nor neostigmine-induced fasciculations appeared in the denervated quadriceps femoris muscle, while a marked increase of fasciculations was present in the nondenervated fasciculating muscles.

These two experiments were conducted simultaneously and were part of a series of long term studies of these patients at weekly intervals. It was apparent from these studies that fasciculations were not immediately abolished by denervation and that a later disappearance of this muscle phenomenon took place. It was obviously necessary to study the problem at shorter intervals.

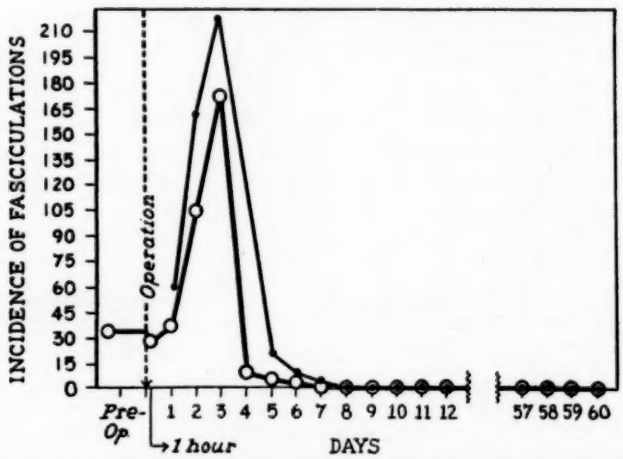

Fig. 2.—Effects of denervation on incidence of fasciculations, as observed at daily intervals in experiment 3. There was a transient increase of fasciculations in the quadriceps femoris muscle after section of the femoral nerve and absence of spontaneous and neostigmine-induced fasciculations on the eighth and on all subsequent days. The break in the base line indicates that no fasciculations were recorded between the twelfth and the fifty-seventh day.

In experiment 3 (fig. 2), after section of the left femoral nerve, daily observations were made for a period of sixty days. There was a striking increase in the incidence of both spontaneous and induced fasciculations on the second and third postoperative days, followed by complete cessation of both spontaneous and induced fasciculations from the seventh day after sectioning.

CONCLUSIONS

Effect of Denervation.—In three separate experiments the denervation of fasciculating human skeletal muscle failed to produce immediate

disappearance of fasciculations. In the single experiment in which daily recordings were made an increase in the number of fasciculations was noted on the second and third days after nerve section, and both spontaneous and neostigmine-induced fasciculations failed to appear after the seventh day following denervation. In the other two experiments, with observations at weekly intervals, fasciculations were present on the fourth and fifth days after denervation but could not be elicited on the eleventh and twelfth days or on subsequent days following nerve section.

The presence of fasciculations during the first seven days after nerve section confirms the opinions derived from the previously reported observations on pharmacologic block of the nerve supply of fasciculating muscle. The very presence of fasciculations in muscle after section of the motor nerve supply of that muscle demonstrates conclusively that the anterior horn cell cannot be the site of origin of fasciculations in muscle, as there is no longer any continuity of conduction pathways between the anterior horn cell and the myoneural junction. There remains as the possible site of origin only the distal portion of the nerve, the myoneural junction and the muscle itself. Since it is unlikely that the nerve fibers themselves could give rise to impulses producing these muscle fiber contractions and since, as was demonstrated in the previous observations,[1] the frequency of fasciculations is influenced by drugs acting at the myoneural junction, the logical deduction is that fasciculations originate in this region.

In these experiments there could be no question of the complete interruption of the motor nerve supply of the denervated muscles. Muscles chosen for study were such that a single nerve contained their entire motor nerve supply. Not only were these nerves sectioned, but a considerable portion of the nerve trunk was excised so that the separation of distal and proximal ends would be greater than that produced by simple section. Thus, any possibility, however slight, of nerve regeneration during the course of the experiments was obviated. The use of coaxial grounded needles insured against the possibility of pick-up from surrounding, nondenervated muscles. In addition to this, it was possible visually to observe gross fasciculations of the denervated deltoid and quadriceps femoris muscles. The continued presence of fasciculations for a period of days after denervation confirms the previous deductions from pharmacologic nerve block and hence indicates the validity of the use of spinal anesthesia or of nerve block in studying this problem.

The ultimate disappearance of fasciculations in denervated muscles raises a vexing point, and one which requires a further consideration of differences and relationships between fasciculations and fibrillations.

Fibrillations Versus Fasciculations.—In many respects the differences between fasciculations and fibrillations are not decisive. Fibrillations are fine, continuous, tremor-like contractions, visible in strong reflected light on the surface of exposed denervated muscle. Fasciculations are grosser contractions, apparent through the intact skin, and appear classically in association with disease of the anterior horn cell. Fibrillations are considered to be contractions of a part of or an entire muscle fiber. Fasciculations are considered to be the contraction of a group of muscle fibers, a single motor unit. The differentiation between these two types of involuntary muscular contraction, as cited, was clarified by Denny-Brown and Pennybacker,[3] who concluded that fibrillations arose at the myoneural junction and inferred that fasciculations arose from the anterior horn cells. However, even they found occasionally in their experiments that fibrillations approached fasciculations in their characteristics. Tower,[4] in her review, concluded that it is uncertain whether a sharp distinction exists between the two phenomena and advocated the utilization of such critical procedures as nerve block to differentiate further between the two states.

Among neurologists there is no clear differentiation between fibrillations and fasciculations, and, indeed, many clinicians and some physiologists employ the terms interchangeably. On the surface the problem would seem to be quite simple, in view of the previously outlined differences, especially since fibrillations occur only after denervation and fasciculations appear in the presence of disease of the anterior horn cells. However, both progressive muscular atrophy and amyotrophic lateral sclerosis are associated not only with diseased neurons of the anterior horn cells but also with a paucity of cells, thus producing essentially a denervation of the corresponding motor units. Viewed from this standpoint, the apparently different etiologic origin of the two phenomena loses much of its importance. The similar site of origin, the myoneural junction, of the two phenomena also tends to lessen the differences between them.

Fibrillations appear in denervated animal muscle in varying periods of from two to eight days after denervation, the longer time intervals occurring with the higher animals. Feinstein, Pattle and Weddell[5] found in a single experiment that it required sixteen days for the development of fibrillations in denervated human muscle. Fasciculations, according to our observations, disappear in human muscle approximately

3. Denny-Brown, D., and Pennybacker, J. B.: Fibrillation and Fasciculation in Voluntary Muscle, Brain **61**:311, 1948.

4. Tower, S.: The Reaction of Muscle to Denervation, Physiol. Rev. **19**:1, 1939.

5. Feinstein, B.; Pattle, R. E., and Weddell, G.; Metabolic Factors Affecting Fibrillation in Denervated Muscle, J. Neurol., Neurosurg. & Psychiat. **8**:1, 1945.

seven days after denervation, while fibrillations appear at a somewhat later date and are permanent. The possibility immediately arises that fasciculations may be multiple, simultaneous fibrillations occurring in the same motor unit. Since fasciculations induced by neostigmine are known to yield antidromic impulses,[6] presumably from the myoneural junction, and since antidromic impulses have been described from peripheral stimulation of a motor nerve, it is conceivable that such impulses could exert a synchronizing effect on the muscle fibrils served by a single motoneuron axon. This could be accomplished either by the effect of antidromic impulses on the motoneuron in the anterior horn cell or by means of an axon reflex, thus not requiring the mediation of the anterior horn cell. In view of the persistence of fasciculations for some time after denervation, antidromic impulses could be effective only as part of an axon reflex. The pronounced decrease in the incidence of fasciculations occurring from the fourth to the fifth day after denervation corresponds well with the anatomic changes occurring in the axons of the peripheral stump of a sectioned nerve. At this stage of denervation the axons have become degenerated to a degree that segmentation occurs, together with inclusion of fragments of the axon with fragments of myelin. In other words, by the time fasciculations disappear in denervated muscle it is unlikely that the peripheral stump of the nerve retains the ability to conduct impulses from the myoneural junction.

The anatomic changes in denervated muscle cannot be correlated temporally with the disappearance of fasciculations. Alterations of muscle striations, sole plate granules and frankly degenerative changes occur much later; and, while subsarcolemmal nuclei show alterations early in the course of denervation, it is difficult to conceive of these alterations having any relevant bearing on the incidence of fasciculations. The determination of chemical alterations in denervated muscle has of necessity been on experimental animals. These studies [4] indicate that within the period of disappearance of fasciculations there occur an increase in calcium and phosphoric acid and a decrease in glycogen, potassium and phosphocreatine. These chemical alterations suggest a biochemical origin of the fasciculations, and the changes in potassium, coupled with the known increase of fasciculations produced by neostigmine indicate that synthesis and destruction of acetylcholine may be concerned with the induction of fasciculations at the myoneural junction.

In experiment 3 the increase of fasciculations during the second and third days after denervation requires further investigation. This was not noted in the other experiments, possibly as a result of too infrequent readings.

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6. Masland, R. L., and Wigton, R. S.: Nerve Activity Accompanying Fasciculations Produced by Prostigmin, J. Neurophysiol. **3**:269, 1940.

SUMMARY

Fasciculations do not arise at the anterior horn cell, since they are present for a time after denervation of the fasciculating muscle. Fasciculations, like fibrillations, originate at the myoneural junction. Fasciculations and fibrillations probably represent the same phenomenon, the only difference being that fasciculations are synchronized fibrillations occurring in the same motor unit. The decrease of fasciculations about four days after denervation correlates with the anatomic changes in the peripheral nerve stump. Fibrillations are probably synchronized into fasciculations by antidromic impulses from the myoneural junction and firing in axon reflex fashion. The disappearance of fasciculations is due to the destruction of the synchronizing pathway when the peripheral stump degenerates.

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DISCUSSION

Dr. Richard Masland, Philadelphia: It is important to emphasize the distinction between fibrillation and fasciculation. In fibrillation the individual muscle fibers contract independently. In fasciculation there is a synchronized discharge of a group of muscle fibers. There is every reason to believe that this synchronization is due to neural activity and represents the response of a motor unit to a nerve impulse.

It has been shown that in the case of the fascicular twitch which follows the administration of neostigmine there is a nerve impulse associated with the contraction. This impulse may arise either through antidromic musculoneural transmission or by direct stimulation of the nerve ending sensitized by the drug (Eccles, J. C.; Katz, B., and Kuffler, S. W.: *J. Neurophysiol.* **5**:211, 1942). When the nerve ending is stimulated, an antidromic impulse is set up; there is an axon reflex, and a motor unit discharge results.

There is a striking similarity between the "neostigmine twitch" and the fasciculation of anterior horn cell disease. Both are inhibited by small doses of curare. The experiments just concluded indicate that each arises at the nerve ending. It is my belief that in each instance the fundamental element is an abnormal excitability of the nerve ending.

In attempting to explain the fact just demonstrated that although the disease is in the anterior horn cell the twitch arises at the nerve ending, it is important to bear in mind that the anterior horn cell includes not only the cell body but the peripheral nerve, which is its axon, and the nerve ending. It is not remarkable, therefore, to discover that a disease which is demonstrated pathologically in the cell body within the spinal cord produces striking physiologic changes in the entire cell. These manifest themselves as an alteration in excitability at one of the more highly specialized portions of the neuron—the nerve ending.

Dr. Richard Masland, Philadelphia: In reply to Dr. Alper's question, Eccles has expressed the opinion that the increased irritability of the nerve ending observed with neostigmine poisoning may be due to prolonged negativity. In view of the striking similarity between the twitch seen with such diseases as amyotrophic lateral sclerosis and the "neostigmine twitch," it is not unreasonable to postulate that the same factor is responsible for both.

Dr. Frederic H. Lewey, Philadelphia: The question of fibrillations or fasciculations is important also from the clinical point of view. A review of the textbooks shows it to be almost an axiom that "fibrillation" is characteristic of a

lesion of the anterior horn cell, in contrast to one of the peripheral nerve. Oscillographic records show that the completely denervated muscle "fibrillates." This is not visible clinically. The first sign of beginning reinnervation of a muscle is the appearance of not yet synchronized, spread potentials, which are now called "fasciculations"! They are visible clinically as what were formerly called fibrillations. No voluntary motion is possible at that stage. The last stage of muscle reinnervation is characterized by the appearance of synchronized action potentials, i. e., spikes, accompanied with the return of voluntary movements. This experience gained from patients with peripheral nerve injuries corresponds to the observations of the authors, with the restriction that in diseases such as spinal progressive muscular dystrophy some units may be diseased and others still functioning well.

Dr. Francis M. Forster, Philadelphia: Our use of the term anterior horn cell should be clarified, for by that term we referred to the cell body and its nucleus, and not specifically to the axonal terminations. The experimental data presented this evening indicate definitely that the impulses giving rise to fasciculations did not originate from the portions of the cells in the ventral horns of the spinal cord. Fundamentally, I do not believe there is any real difference of opinion between ourselves and Dr. Masland. Our studies did not include patients with myopathies. However, the myopathies are not always sharply delineated, and the occurrence of clinical or pathologic evidence of involvement of the cord with the myopathies is by no means rare.

TOXICITY OF QUINACRINE (ATABRINE) FOR THE CENTRAL NERVOUS SYSTEM

III. An Experimental Study on Human Subjects

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A METHOD of detecting and measuring the toxic effects of drugs on cerebration and its use in a preliminary investigation of the toxicity of quinacrine (atabrine) are presented. The procedure is simple and consists in principle in comparing the intellectual functioning of subjects while taking the drug and when free of the drug. Groups of subjects receiving different doses of quinacrine hydrochloride and with varying serum levels of the drug were tested to gain an approximate estimate of the dose which tends to be toxic for human subjects.

The study was undertaken when it was observed, during the treatment of many thousands of patients for malaria, that the most serious toxic effect of quinacrine was the occurrence of toxic psychoses. This complication was seen most often after excessive doses. Massive quinacrine therapy had been instituted on the island on which we were stationed to determine whether the production and maintenance of a high quinacrine level in the serum would check the recurrence of tertian malaria. The sole serious limitation to the quantity of quinacrine which could be given appeared to be the relationship between the rapidity of administration of large doses and the occurrence of confusion or overt psychoses. As the treatment by massive dosage brought little, if any, benefit, the experiment was abandoned. However, the experience indicated that as the important toxic effect of quinacrine was on the central nervous system, the limitations of dosage should be determined in terms of the effect of the drug on the central nervous system. A means was therefore sought which would permit the measurement of the effects of the drug on mental functioning.

It is well to clarify the meaning of toxicity as applied to quinacrine. The risk to be taken in the use of a drug is proportionate to the benefits to be derived. The toxic dose cannot be determined according to fixed

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standards. If massive dosage of quinacrine decreased the rate of recurrence of tertian malaria markedly, the risk of an occasional quinacrine psychosis might well be considered worth while. The balancing of an optimal therapeutic dosage would then be a difficult matter. As it now appears that heavy dosage is of little benefit, the problem is not difficult. The dose is to be maintained below that which will produce toxic effects. The determination of toxic levels of the drug, which is the purpose of this study, would be a matter of only pharmacologic interest if it were not for the problem of the toxic psychoses.

Quinacrine psychoses have been reported by a number of observers. Experiences on this island with 28 cases of toxic psychosis [1] and 7 cases of convulsive seizures [2] due to quinacrine among approximately 30,000 patients treated for malaria have been reported in previous papers. Psychoses were infrequent when conventional therapy (2.1 or 2.8 Gm. of quinacrine hydrochloride in seven days) was used but increased in frequency when massive therapy (1.4 Gm. in twenty-four hours; 3.8 or 4.8 Gm. in seven days, and so on) was employed. With cessation of heavy dosage, quinacrine psychoses again became a rarity, although the number of patients treated remained unaltered. It was noted that, in addition to the patients with frank psychoses, a fair number of the men who received the large amounts of quinacrine complained of feeling confused or intoxicated. Confusion is basic to the toxic psychoses and connotes impairment of mental functioning. It was believed that if the mentation of some patients were sufficiently disturbed by the quinacrine to produce confusion that was perceptible, either objectively or subjectively, the utilization of refined means of testing would uncover lesser degrees of impairment in a larger proportion of the patients.

It happened that 2 patients who became psychotic under massive quinacrine therapy had been given intelligence tests a day or two before they had the onset of psychosis, but after they had taken a large quantity of quinacrine. The severity of the mental deficiency that existed in both patients was estimated erroneously, for the patients showed a significant increase in their mental ages when retested after recovery from the psychosis and after quinacrine had been withdrawn for some time. For 1 of the patients the score on the Stanford-Binet test shifted from a mental age of $6\frac{9}{12}$ years to one of $9\frac{3}{12}$ years, and for the other, from a mental age of $9\frac{9}{12}$ years to one of $11\frac{8}{12}$ years; and the score on the Kohs block test given the second patient shifted from a mental age of 6 years to $10\frac{11}{12}$ years. The presence of impaired intellectual functioning prior to the onset of the psychoses in these patients sug-

1. Newell, H. W., and Lidz, T.: The Toxicity of Atabrine to the Central Nervous System: I. Toxic Psychoses, Am. J. Psychiat., to be published.

2. Newell, H. W., and Lidz, T.: The Toxicity of Atabrine to the Central Nervous System: II. Convulsions, Am. J. Psychiat., to be published.

gested that transient impairments due to subclinical confusion might well be found in other patients receiving massive doses of quinacrine.

SELECTION OF THE TEST PROCEDURE

The comparison of intellectual functions in a subject at any two times may be carried out in a number of ways, and emphasis may be placed on various functions of the intellect. There are limitations in the choice of the procedure which must be considered. It is realized from the study of deteriorations following structural damage to the brain that such changes, particularly when of recent origin, are not always apparent. Some tests of mental capacity may fail to reveal the defect, for the patient retains information, habitual modes of thinking and patterns of behavior which had been acquired when the intellect was intact. Learned material which can be given without complicated reflective or synthetic thinking may remain at the disposal of the patient. Therefore, such methods of measuring intelligence as the Binet test, which measures to a large extent what the subject has learned by means of his intelligence, are unsuited to the study of deteriorations. It is necessary to test the ability for active mentation at the moment, utilizing a method which permits a minimum of reliance on knowledge and behavioral patterns acquired in the past. For group studies, it is necessary to select a procedure which yields numerical data that can be utilized statistically.

The choice of a suitable procedure has been discussed in detail by Lidz, Gay and Tietze,[3] in an article on the application of the Kohs block test to the study of organic deficit states. The Kohs block test seems equally advantageous for the study of transitory impairment of the intellect. It is singularly free from the influence of past experience; it is a well standardized and highly reliable procedure, suited to adult testing; it is well graded and measures a wide range of intelligence levels; retesting with the same procedure does not produce significant alterations in the score, and there is little room for subjective error in the results, which are scored in numerical terms. Although several other procedures were utilized at the start of the experiment, particularly memory tests, it was found that whenever significant results were obtained they were also to be noted in the Kohs block test. The discussion of the experimental results will therefore be limited to this test.

The nature of the Kohs block test and the method of administration will be outlined briefly. A complete discussion of the test has been presented by Kohs,[4] but the procedure has been modified slightly.

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3. Lidz, T.; Gay, J. R., and Tietze, C.: Intelligence in Cerebral Deficit States and Schizophrenia Measured by Kohs Block Test, Arch. Neurol. & Psychiat. **48**: 568 (Oct.) 1942.

4. Kohs, S. C.: Intelligence Measurement, New York, The Macmillan Company, 1923.

The test material consists of 16 identical 1 inch (2.54 cm.) color cubes and 17 standardized designs of graded complexity drawn on separate cards to a 1 : 4 scale. Each cube has four solidly colored sides—blue, red, white and yellow; a fifth side is divided diagonally into red and white, and a sixth, into blue and yellow. It is explained that the 16 cubes are identical, and the various sides are pointed out. A simple sample design is presented to the subject, who is requested to reproduce the pattern with the upper surfaces of the cubes. The subject is given all 16 blocks. It is explained that only 4 cubes are needed to form the simple pattern, but more will be necessary for some designs. The method of forming the sample pattern is demonstrated if necessary. The subject is then requested to make the first design as rapidly as possible and is then offered one design after another until failure occurs on three successive patterns. If the subject does not realize that more than 4 blocks are needed to form the tenth design, he is told. The time permitted for the completion of each pattern is found on the card, but precise time is recorded, as bonus scores are given for rapid completions.

The scoring and calculations of the mental age are made according to the tables of Kohs,[4] but the number of moves made in the completion of a pattern is not taken into consideration, as many workers have found it to be a complicating factor that does not increase the accuracy of the procedure appreciably. A perfect score is equivalent to a mental age rating of 20 years, and the lower limit, inability to complete the simplest design, indicates a mental age of less than 5½ years.

As the test was to be given twice to the same subject, two sets of design cards were used to minimize the learning factor. The second set consisted of the same designs but with the color scheme reversed. The red and white patterns were made blue and yellow and vice versa except for the seventeenth design, which would be simplified by reversal of the color scheme. The first control group was divided in half, and each half was tested with opposite sets of patterns and retested with the other set. No appreciable difference between the sets of patterns was found.

The results of each test were calculated in years of mental age, and the difference between the two tests was calculated in months of mental age.

PLAN OF THE EXPERIMENT

The simplest and most satisfactory approach would be to determine the mental ages of a group of subjects with the Kohs block test, administer quinacrine and retest with the Kohs block test after a given amount of the drug had been taken or a definite serum quinacrine level had been attained. A fall in the mental age on the retest of more than 1 year or 18 months would be an indication of impaired mentation, as subjects tend to gain a higher score on the retest and rarely show a decline in score of as much as 18 months. The study was carried out under conditions which imposed limitations that complicated the procedure.

It did not appear wise or practicable to administer heavy doses of quinacrine to volunteers. The experimental subjects were patients with recurrences of tertian malaria who received the quinacrine therapeutically. It was necessary, therefore, to administer the first Kohs test when the patients were receiving the drug and to retest later, when the patient had ceased taking quinacrine and had been free

from the drug for some time. A pronounced increase in score would indicate that impairment existed when the first test was given.

Familiarity with the procedure, rather than elimination of the toxic agent, would then account for some of the improvement on the second test. The limitation was overcome and controlled by measuring the improvement shown by a group of normal subjects, persons who did not take the drug and did not have malaria. The presence of malaria constituted a second factor which might influence the results, for it was possible that the malaria might cause a transient impairment of mental functioning even though the subjects were afebrile and had recovered from the attack when tested. A second control group was established which was composed of patients who had malaria but who were treated with quinacrine in a dose which would be unlikely to have an effect on the central nervous system. Tests on the two control groups yielded similar results, indicating that the second group was not affected by the small dose of quinacrine, as will be seen later. The results of the testing of the experimental subjects were then analyzed by comparison with the data for the two control groups.

TABLE 1.—*Scores on Kohs Block Tests for 30 Control Subjects Who Received No Quinacrine*

Number	Test Score *	Retest Score †	Difference in Score (Mo.)	Number	Test Score	Retest Score	Difference in Score (Mo.)
1	13-7	12-7	−12	16	12-8	14-3	+19
2	13	12-7	− 5	17	16	17-8	+20
3	11-3	10-11	− 4	18	13-5	15-3	+22
4	10-4	10-2	− 2	19	18	19-10	+22
5	20	....	....	20	18	20	+24
6	20	....	....	21	14-2	16-6	+28
7	20	....	....	22	17-6	19-10	+28
8	19-3	....‡	....	23	13-11	16-4	+29
9	9-3	9-6	+ 3	24	15-9	18-2	+29
10	17-8	18	+ 4	25	14	16-8	+32
11	17-6	18	+ 6	26	12	14-11	+35
12	12-3	13-1	+10	27	16	18-11	+35
13	11-2	12	+10	28	16-6	20	+42
14	18-11	20	+13	29	11-4	14-11	+43
15	14-2	15-3	+13	30	15-5	19-8	+51

* Mental age in this table, and in subsequent tables, is expressed in years and months.
† Patients were retested after an interval of seven days.
‡ Subjects who attained very high scores on the first test were not always retested.

A third limitation may have detracted slightly from the accuracy of the experimental results; but as the effect would be to minimize significant data rather than to exaggerate them, it is not of great importance. The need for hospital beds required that the retests be carried out as soon as possible. The subjects were retested one week after the cessation of quinacrine therapy, and there were indications that the effects of the drug had not disappeared completely by that time. A small group of subjects and controls were tested for a third time after an interval of one month to estimate the significance of the error.

The following groups of subjects were tested:

GROUP 1.—This series consisted of 30 normal subjects. They were members of the hospital detachment who had never had malaria and had never received quinacrine. There was an interval of seven days between the two tests. The series formed the control showing the increase in the score due to familiarity when retesting was done after an interval of seven days. The results of the testing are shown in table 1. Ten subjects were retested a second time, a month after the first test was given.

GROUP 2.—This series consisted of 27 patients who were treated for malaria with quinacrine hydrochloride, 0.1 Gm. three times a day for seven days, a total of 2.1 Gm. The patients were tested on the seventh day of treatment and were retested after an interval of seven days. Serum quinacrine levels were obtained on 26 patients on the sixth, seventh, or eighth day.[5] The subjects were all afebrile, asymptomatic and ambulatory when tested. The series formed a control against the possibility that the malaria influenced mental functioning. The results of the testing are to be found in table 2.

GROUP 3.—The series consisted of 31 patients who were treated for malaria with quinacrine hydrochloride according to a schedule of 0.3 Gm. three times a day for three days, followed by a regimen of 0.2 Gm. three times a day for three days, making a total dose of 4.5 Gm. in six days. The patients were tested on the sixth day of treatment and were retested after an interval of seven days. Serum quinacrine levels were obtained on 29 patients some time between the fourth and the eighth day (23 patients on the fourth day). The patients were

TABLE 2.—*Scores on Kohs Tests for Control Group of 27 Subjects Who Received 2.1 Gm. of Quinacrine Hydrochloride in Seven Days*

Number	Test Score *	Retest Score †	Difference in Score, Mo.	Serum Level, Micrograms per 100 Cc.‡	Number	Test Score	Retest Score	Difference in Score, Mo.	Serum Level, Micrograms per 100 Cc.
1	12-6	11-5	—13	3	15	14-10	16-4	+18	4
2	12-3	11-4	—11	7	16	12-7	14-3	+20	4
3	14-3	13-7	— 8	3	17	14-2	16	+22	4
4	14-11	14-7	— 4	3	18	11-11	13-11	+24	5
5	20	....	....	4	19	10-4	12-9	+29	3
6	19-8	....	....	5	20	13-2	15-7	+29	5
7	18	....	....	2	21	14-6	17	+30	3
8	18-2	....	....	1	22	11-6	14	+30	5
9	19-6	....	....	3	23	13-11	16-8	+33	8
10	17-10	....	....	6	24	8-10	11-9	+35	..
11	19-8	....	....	5	25	16-6	19-6	+36	8
12	15-5	16-7	+14	5	26	16-7	19-8	+37	6
13	12	13-3	+15	10	27	15-7	19-3	+44	3
14	16-5	17-10	+17	7					

* Patients were tested on the seventh day of treatment.
† Patients were retested after an interval of seven days.
‡ Serum levels were determined on the sixth, seventh or eighth day.

all asymptomatic and ambulatory when tested. This series forms the major experimental group. The results of the testing are to be found in table 3. Ten patients were retested a second time, one month after the initial test.

GROUP 4.—A series of 10 patients form a subsidiary experimental group, as the experiment was interrupted before the series could be completed. The patients were treated with quinacrine hydrochloride, 0.1 Gm. three times a day for twelve weeks. They were tested during the ninth week of treatment, after they had received approximately 17 Gm. of quinacrine hydrochloride. Serum quinacrine levels were obtained at the time of testing. The patients were tested again two weeks after the termination of treatment, and five weeks after the first

5. Determinations of the serum quinacrine level were provided by Capt. Roger A. Lewis, Medical Corps, Army of the United States, and were made by his method, which has been well standardized (Lewis, R. A.: J. Lab. & Clin. Med. **29**:1303 [Dec.] 1944).

test was made. The series of tests was intended to determine whether large quantities of quinacrine given in a dosage which did not produce a very high serum level could cause toxic symptoms. The group is small and will not enter into consideration except as the data were used as a further check on the results

TABLE 3.—*Scores on Kohs Test for Experimental Group of 31 Subjects Who Received 4.5 Gm. of Quinacrine Hydrochloride in Six Days*

Number	Test Score *	Retest Score †	Difference in Score, Mo.	Serum Level, Micrograms per 100 Cc.‡	Number	Test Score	Retest Score	Difference in Score, Mo.	Serum Level, Micrograms per 100 Cc.
1	11-6	10-6	—12	12	17	11-2	12-11	+21	23
2	14-4	13-9	— 7	11	18	6	8	+24	20
3	19-3	....	....	15	19	11-2	13-5	+27	20
4	19	....	....	11	20	15-5	18	+31	20
5	10-5	10-7	+ 2	10	21	9-5	12	+31	25
6	19-8	20	+ 4	10	22	13-10	17-4	+42	20
7	10-9	11-6	+ 9	15	23	16	19-10	+46	18
8	17-9	20	+27	10	24	15-3	19-3	+48	18
9	12	14-6	+30	10	25	12-4	16-4	+48	30
10	12	14-9	+33	9	26	12-5	16-11	+54	18
11	11-6	15-6	+48	12	27	10-7	15-4	+57	20
12	11-1	10-8	— 5	25	28	13-8	19-8	+72	20
13	9-5	9-10	+ 5	18	29	11-9	18	+75	28
14	12-2	12-10	+ 8	20	30	20	....	....	..
15	19	19-8	+ 8	20	31	15-8	18-5	+33	..
16	11-4	12-10	+18	20					

* Patients were tested on the sixth day of treatment.
† Patients were retested after an interval of seven days.
‡ Serum levels were determined between the fourth and the eighth day (23 patients on the fourth day).

TABLE 4.—*Scores on Kohs Test for Subsidiary Experimental Group Who Received 0.3 Gm. Quinacrine Hydrochloride Daily for Twelve Weeks*

Number	Test Score *	Retest Score †	Difference in Score, Months	Serum Level, Micrograms per 100 Cc.‡
1	12-7	11-3	—16	7
2	13-6	12-9	— 9	15
3	19	....	....	11
4	14-3	14-5	+ 2	7
5	17-4	17-11	+ 4	6
6	16-7	17-6	+11	10
7	15-11	17-5	+18	9
8	14-10	16-7	+21	..
9	10-6	12-4	+22	8
10	7-5	10	+31	6

* Patients were tested during the ninth week of treatment.
† Patients were retested during the fourteenth week.
‡ Serum levels were determined during the ninth week.

obtained in the testing of the other groups of patients. The results are to be found in table 4.

In all groups, subjects who attained very high scores on the first test were not always retested, as it was apparent that no measurable deficit had resulted from the quinacrine therapy. The lapse in technic had no appreciable effect

except in group 2, in which the mean increase in mental age on the retest may be 1 to 2 months lower than it should be, an error without significance in the results of the study.

ANALYSIS OF DATA

The experimental data concerned with the first three groups will first be examined on the basis of the dose of quinacrine and thereafter on the basis of the serum quinacrine levels.

TABLE 5.—*Means for Scores Obtained by Three Groups of Subjects*

	Mean Mental Age Test I, Yr.	Mean Mental Age Test II, Yr.	Mean Difference Between Tests, Mo.
Group 1 (no quinacrine).....	15.1	16.5	16.4
Group 2 (2.1 Gm. quinacrine).....	15.0	16.2	14.7
Group 3 (4.5 Gm. quinacrine).....	13.4	15.5	25.1

The means for the scores obtained on the tests by each group of subjects are given in table 5.

It is seen that the means for groups 1 and 2 are practically identical. The means for group 3 differ from those for the other two groups, the scores being lower on the tests and the difference between the scores on the two tests being greater. The difference appears suggestive but cannot be considered of statistical significance. However, a significant statistical variation between the mean differences in the scores could not be anticipated unless a large majority of the subjects who received 4.5 Gm. of quinacrine hydrochloride had shown a pronounced toxic effect from the drug. An analysis of the distribution of the scores in the three groups yields more interesting information.

Chart 1 shows the distribution of the scores obtained on the two tests by the subjects in groups 1 and 2. The chart is a scatter graph of the mental age levels obtained on the first test plotted against the mental age levels obtained on the second test. The scatters for the two groups are almost identical. Chart 2 shows the scatter of the mental ages on the test and on the retest obtained by the subjects of group 3. The tendency toward a greater increase in the mental age on the retest in group 3 than in groups 1 and 2 is apparent. Whereas chart 1, combining the values for 57 patients in groups 1 and 2, shows only 1 subject with an increase in mental age of 4 years or more on the retest, 7 of the 31 patients in group 3 showed an increase of 4 years or more.

The differences in the groups can be seen more easily from the study of chart 3. This chart is a cumulative frequency graph which shows the percentage of patients in each of the three groups that improved up to any given number of months on the retest. The curves for the first two groups, like the means and the scatter, are remarkably similar, indicating that the presence of malaria and the administration of 2.1 Gm. of quin-

acrine hydrochloride had no effect on the mental functioning, at least as measured by the technic. The curve for the patients given 4.5 Gm. of quinacrine hydrochloride differs. Not only do the values for some patients fall outside the limits of the curves for group 1 and group 2, but there is a generalized shift. The differences are summarized in table 6.

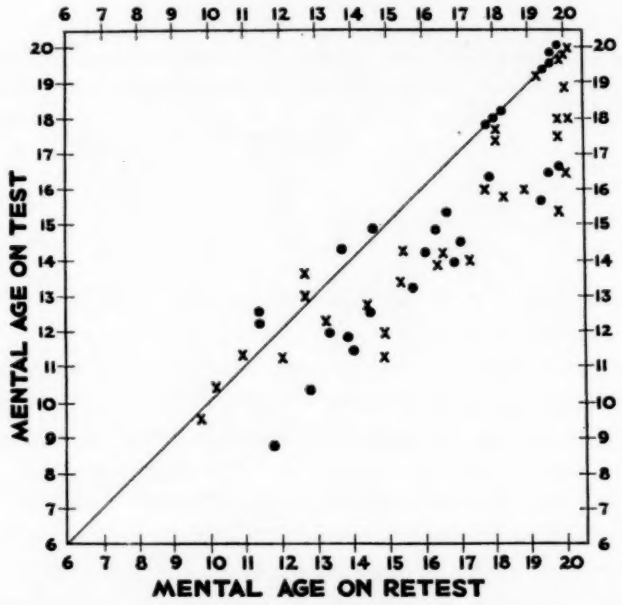

Chart 1.—Correlation of mental ages obtained on Kohs block test and on a retest after seven days for group 1 (30 subjects, normal controls) and for group 2 (27 subjects given 2.1 Gm. of quinacrine hydrochloride).

The values for the controls are shown by crosses; those for the patients given quinacrine, by solid circles.

TABLE 6.—*Distribution of Improved Scores for Three Groups of Subjects*

Increase in Score (Months) on Retest of	Group 1 No Quinacrine, Per Cent	Group 2 2.1 Gm. of Quinacrine, Per Cent	Group 3 4.5 Gm. of Quinacrine, Per Cent
18 or more	50	48	61
24 or more	37	37	55
30 or more	20	26	45
36 or more	10	11	29
42 or more	10	4	29
48 or more	3	0	23
54 or more	0	0	13
60 or more	0	0	6

An improvement in the mental age of 48 months or more on the retest is seen to be decidedly unusual in the controls, whereas 23 per cent, or 7 subjects, who received 4.5 Gm. of quinacrine hydrochloride showed such improvement, indicating that it is extremely likely that the quinacrine had impaired their mentation when they were first tested.

The higher percentage of subjects in group 3 that showed large discrepancies in the results of the two tests suggests that a large proportion of the group experienced some impairment due to the drug. Group 3 is obviously not a pure group; that is, some subjects seemed to have suffered from the toxicity of the quinacrine and others not. This might be anticipated, as it was apparent clinically that the dose could not be higher than that bordering on the toxic.

If the hypothesis is accepted tentatively that the tests indicate that a dose of 4.5 Gm. affected some subjects and not others, several explanations may be offered. There may have been differences in absorption or excretion, with variations in serum levels, or differences in individual sensitivity; or other factors, such as spinal fluid levels, may have

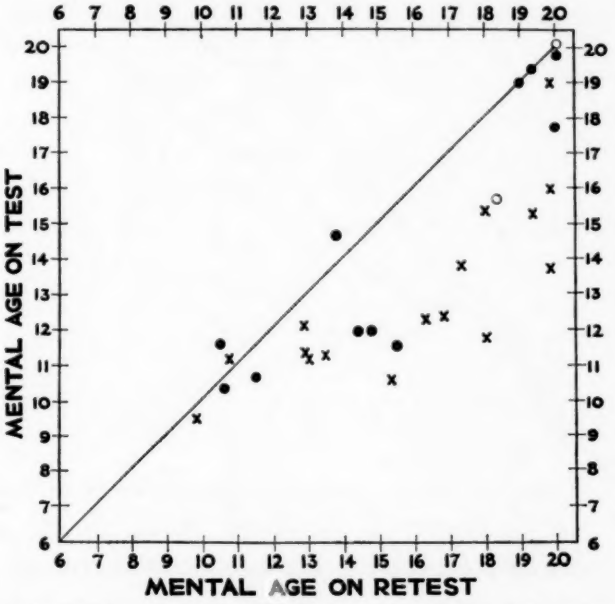

Chart 2.—Correlation of mental ages on Kohs block test for group 3 (31 subjects) tested on the sixth day of treatment with 4.5 Gm. of quinacrine hydrochloride and retested after seven days. The group is subdivided into subjects with high (18 micrograms per hundred cubic centimeters or more) and subjects with low (less than 18 micrograms per hundred cubic centimeters) serum quinacrine levels.

The values for the subgroup with higher serum quinacrine levels are shown by crosses; the values for the subgroup with lower serum quinacrine levels, by solid circles, and no determination of the serum quinacrine level is shown by a hollow circle.

to be taken into consideration. Analysis of the serum levels not only gives further information but tends to confirm the efficiency of the technic.

ANALYSIS OF DATA ACCORDING TO SERUM LEVELS

The compilation of data according to the quinacrine dose is an arbitrary procedure which is based on the knowledge, gained from a large

group of patients, that given schedules of therapy tend to produce serum quinacrine levels within certain limits. There is considerable variation in the serum levels in different subjects under the same regimen of treatment. It seems well to attempt to correlate the results of the mental testing with the measure of the toxic agent in the circulation.

Serum quinacrine levels were obtained on 26 of the 27 subjects in group 2 on the sixth, seventh or eighth day. It is known that there is little variation in serum levels during the last days of the course of treatment. The serum levels varied from 1 microgram (0.001 mg.) to 10 micrograms (0.010 mg.) per hundred cubic centimeters, with a mean level of 4.7 micrograms (0.0047 mg.) per hundred cubic centimeters. As the results of the mental tests showed no toxic effect, it is highly

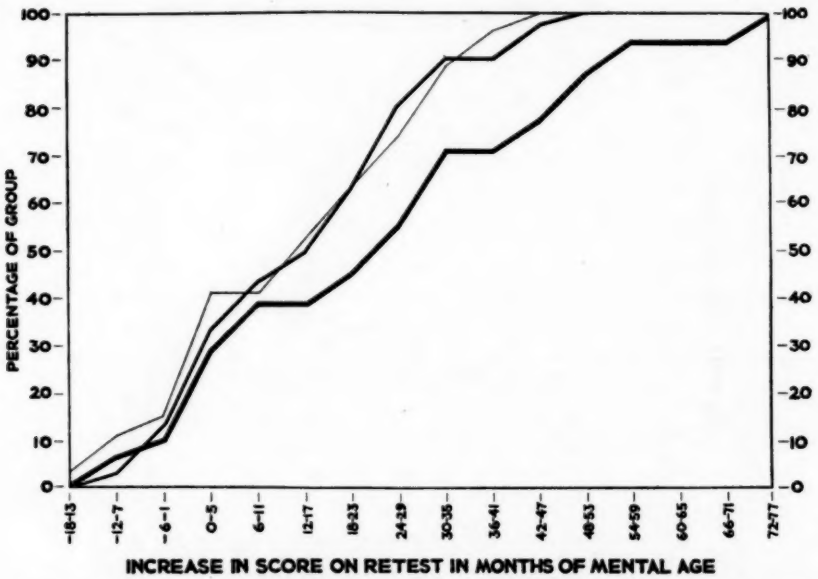

Chart 3.—Cumulative frequency graphs comparing the mental age scores for group 1 (normal controls), group 2 (patients receiving 2.1 Gm. of quinacrine hydrochloride) and group 3 (patients receiving 4.5 Gm. of quinacrine hydrochloride). These curves show the percentages of subjects in each group who showed improvement up to any given number of months of mental age on the retest. The greater the improvement on the retest, the more likely that impairment existed when the first test was given.

The curve for group 1 is shown by a medium heavy line; the curve for group 2, by a light line, and the curve for group 3, by a heavy line.

probable that these levels are not toxic to human subjects. A further check was made by dividing the group into upper and lower halves, 13 patients having serum levels above the mean and 13 patients below. The mean increment in score between the tests for the 26 subjects was 13.9 months. The 13 patients with serum levels below 4.7 micrograms per hundred cubic centimeters had a mean increase of 10.6 months, whereas the 13 patients with the higher serum levels had a mean increase

of 17.2 months on the retest. Although this may indicate that the patients with the higher serum quinacrine levels may have had a slight toxic effect from the drug, the difference is well within the limits of experimental error. The mean increase in the score of 17.2 months is approximately the same as that shown by the controls in group 1.

Serum quinacrine levels were obtained on 29 of the 31 subjects in group 3, who had received 4.5 Gm. of quinacrine hydrochloride. The levels were obtained between the fourth and the eighth day, for 23 of the 29 patients on the fourth day. Although these data are not as satisfactory as though the serum levels had been obtained at the time of the mental testing, it is known that the serum level remains relatively constant between the fourth and the eighth day under this thera-

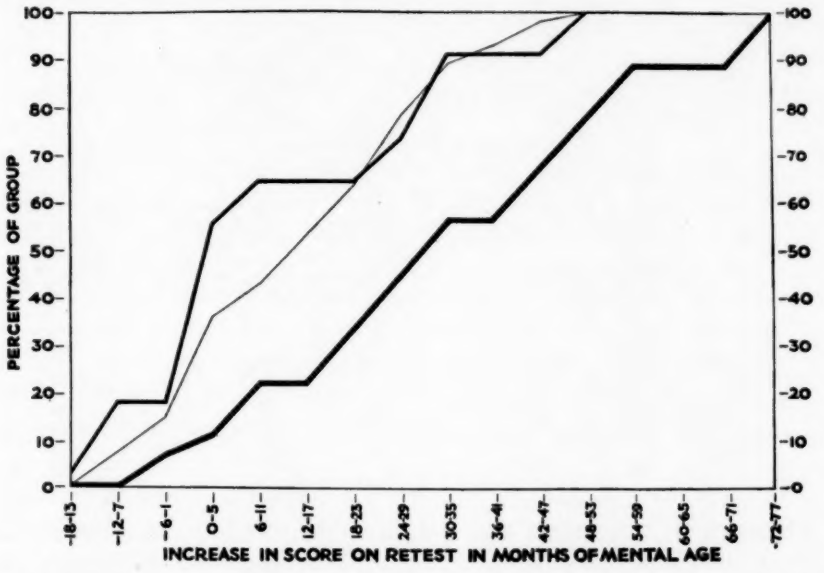

Chart 4.—Cumulative frequency graphs comparing curves for the mental age scores for two subgroups of group 3 (patients given 4.5 Gm. of quinacrine hydrochloride) having serum quinacrine levels above (heavy line) and below (medium line) 18 micrograms per hundred cubic centimeters, respectively, and a normal curve (light line) constructed by combining the scores for groups 1 and 2.

peutic regimen. The serum levels varied from 9 to 30 micrograms per hundred cubic centimeters, with a mean level of 18.2 micrograms per hundred cubic centimeters. Eleven patients had levels of less than 18 micrograms per hundred cubic centimeters (actually 15 micrograms or less), and 18 patients had levels of 18 micrograms per hundred cubic centimeters or above. The mean increment in mental age on the retest for the entire 29 patients was 25.7 months. The 11 patients with the lower levels showed a mean increase of 12.4 months, whereas the patients with the higher levels showed a mean increase of 33.9 months on the

retest. The difference between the means is 21.5 months, a difference which verges on being statistically significant.

Examination of chart 2 shows the difference in scatter in the two subgroups of group 3. It is seen that 6 of the 7 patients who showed an increase in mental age of 48 months or more on the retest had high serum levels, and the tendency for the subjects with high serum levels to show the greater increases in score is apparent. Chart 4 shows the cumulative frequency curve for the subjects in group 3 with serum levels of 18 micrograms per hundred cubic centimeters or more, contrasted with a curve for the subjects with the lower levels and with a curve for the controls, groups 1 and 2 combined. The curve for the subjects with the lower levels runs close to the control curve, whereas the curve for the subjects with the higher serum levels runs a widely separated course, as summarized in table 7.

TABLE 7.—*Distribution of Improved Scores for Subjects with Serum Quinacrine Levels Above and for Those Below 18 Micrograms per Hundred Cubic Centimeters*

Increase in Score on Retest of	Combined Controls (Groups 1 and 2) 57 Patients, Per Cent	Serum Levels Below 18 Micrograms per 100 Cc., 11 Patients, Per Cent	Serum Levels 18 Micrograms per 100 Cc. or Above, 18 Patients, Per Cent
18 or more	49	36	88
24 or more	37	36	77
30 or more	23	27	66
36 or more	11	9	44
48 or more	2	9	33
54 or more	0	0	22

Although it is apparent that not all subjects with serum quinacrine levels of 18 micrograms per hundred cubic centimeters or higher show definite toxic effects on mentation, it is seen that the "impurity" of the curve for the entire group 3, as shown in chart 3, has been clarified to a large extent by the division of the group according to serum levels. The results of the testing of these small groups of patients indicates fairly definitely that, whereas serum quinacrine levels of 18 micrograms per hundred cubic centimeters and above are likely to result in toxic impairment of mentation that is measurable, levels of less than 18 micrograms per hundred cubic centimeters appear to be unlikely to cause impairment of any measurable proportions.

It was assumed in the experimental procedure that if toxic effects of quinacrine were found they would have cleared by the time of the retesting, seven days after the cessation of quinacrine therapy. The amount of the drug in the serum had fallen to a negligible level by this time. There is some evidence, which needs further checking, that the toxic

influence of the drug does not completely disappear so rapidly. This may be due to the deposition of the quinacrine in the cells or in the spinal fluid or to injury to the cells. Ten subjects were retested a second time one month after cessation of treatment. The subjects were selected for retesting because they had not shown a mental age on the second test which was as high as had been anticipated from measuring the intelligence with a vocabulary test. The rationale for this assumption will not be discussed here, as it is extraneous to the experiment; but a discussion of the problem may be found elsewhere.[3] Ten control subjects from group 1 were also tested for a third time. The controls showed a mean increase in score of 9.7 months between the first and the second retest, whereas the subjects who had received 4.5 Gm. of quinacrine hydrochloride showed a mean increase in mental age of 23.2 months. The difference is sufficient to indicate that the results of the experiment may have been somewhat more significant if the retesting had been carried out at a longer interval after cessation of quinacrine therapy.

The data on group 4, which consisted of the 10 patients who had received 0.3 Gm. of quinacrine hydrochloride daily for nine weeks before being tested, will not be analyzed in detail, as the group is too small. However, the results afford a check on the main experiment. Serum quinacrine levels were obtained on 9 patients at the time of testing. The serum levels ranged from 6 to 11 micrograms per hundred cubic centimeters, with a mean level of 8.8 micrograms per hundred cubic centimeters. The difference between the mental ages on the test during the ninth week of treatment and the retest, five weeks later, ranged from — 16 to 31 months, with a mean of 7 months. The results are compatible with those obtained for the control groups. The lesser mean difference may be due to chance but more probably is to be explained by the fact that the retesting was carried out five weeks after the original test instead of just one week later, as in the control groups, a condition which lessened the importance of the learning factor. This incomplete experiment indicates that the total dose of quinacrine is not a significant factor, for these patients had received over 17 Gm. of the drug when they were first tested. It tends to substantiate the evidence that levels below 15 micrograms per hundred cubic centimeters do not cause measurable impairment of mental functioning.

COMMENT

The experiment which is reported was originally planned as a preliminary procedure to test the method as well as the impression gained clinically that some patients who were being treated with massive amounts of quinacrine exhibited impairment of mental functioning. The fortunes of war interrupted further experiments in which the slight diffi-

culties in methodology were corrected and precluded the possibility that we should be able to carry the investigations to a more definitive termination. The results of the preliminary investigation appear sufficiently decisive to indicate that the technic is satisfactory and to provide additional knowledge of the toxicity of quinacrine for human beings.

The technic appears satisfactory, as tests on two separate control groups yielded almost identical results, whereas the scores for the experimental group, in which there was reason to believe, a priori, that the efficiency of mental functioning declined, indicated that some patients suffered such impairment.

A comparison of the data assembled indicates that the conventional quinacrine dose of 2.1 Gm. given in seven days does not exert a toxic effect on mental functioning but that 4.5 Gm. given in six days is likely to cause impairment which occasionally is rather pronounced. Further analysis of the data suggests strongly that there is a relationship between the serum quinacrine level and the deterioration of intellectual functioning. Tests on the group of subjects with serum quinacrine levels of 18 micrograms (0.018 mg.) or more per hundred cubic centimeters yielded results which were definitely abnormal, whereas all groups of subjects with lower serum levels gave results which closely approximated those for the control group which received no quinacrine.

The study was motivated by the desire to clarify the problem of the quinacrine psychoses. The bulk of the psychoses which were observed on this island occurred during or after the administration of quinacrine in a dosage which was much heavier than that employed in conventional therapy. It is seen that a dosage which is sufficient to produce high serum quinacrine levels causes impairment of thinking which is at times considerable. As toxic psychoses are accompanied with, and perhaps caused by, mental confusion, it is to be anticipated that amounts of quinacrine which cause pronounced intellectual impairment will occasionally produce confusion sufficient to cause behavioral abnormalities. However, cases in which quinacrine psychoses followed conventional therapy have been reported and have been seen on this island, though extremely rarely. The etiologic factor in these cases has not been elucidated. It is possible that the patients have an idiosyncrasy to the drug and become confused even when the serum level is low. However, it is known that a rare subject will have a serum level in the neighborhood of 18 micrograms per hundred cubic centimeters after the administration of 0.3 Gm. of quinacrine hydrochloride for six or seven days. It is possible that it is these subjects, who vary from the normal in rates of absorption and excretion, who may become psychotic on treatment with a conventional dose. This matter, which is of interest to the problem of idiosyncrasy to drugs in general, cannot be decided until serum levels can be determined for such patients.

The experimental results confirm the clinical impressions concerning the toxicity of quinacrine. Although quinacrine is toxic to the central nervous system, there is a wide margin of safety, and it is unlikely to exert any toxic effect whatever on the mental processes when given in conventional doses. If the experiences on this island are confirmed elsewhere, the risk entailed in producing very high serum levels is unnecessary, for the efficacy of quinacrine is not increased by such a method of treatment.

SUMMARY

A method of detecting and measuring the toxic influence of drugs on mental activity by means of the Kohs block test is presented, and the rationale of the procedure is discussed. The technic was applied to the study of the toxicity of quinacrine (atabrine) because the most significant toxic effect of the drug, as seen in the treatment of many thousands of patients for malaria, was the occurrence of toxic psychoses. A preliminary experiment was carried out in the determination of the dose of quinacrine which is toxic to the central nervous system. The results indicate that quinacrine given in a conventional dosage of approximately 2.1 Gm. in seven days causes no toxic effect, but when 4.5 Gm. is given in six days a number of subjects show impairment of mental functioning. Correlation of the results of the mental testing with serum quinacrine levels indicates that serum levels above 18 micrograms (0.018 mg.) per hundred cubic centimeters tend to be toxic, whereas subjects with lower serum levels showed no deviation in intellectual functioning from that of normal controls who had received no quinacrine. The toxic levels are rarely found in patients treated conservatively. The experimental results are in accord with the clinical observations that toxic psychoses rarely occur except when massive quinacrine dosage is employed and that, while a fair number of patients receiving massive doses complain of feeling confused or intoxicated, patients under conservative treatment rarely present such complaints.

The results of the study of quinacrine toxicity suggest that the method evolved offers a new means of studying the effect of drugs on mental activity and of defining the optimal dosage when the effect on cerebration is important.

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RING SCOTOMA AND TUBULAR FIELDS

Their Significance in Cases of Head Injury

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AND
PHARMACIST'S MATE THIRD CLASS H. L. TEUBER, U.S.N.R.*

IN EVALUATING a patient's complaints, one is always confronted with the question whether the symptoms are "organic" or "psychogenic." If there is a history which is typical of a well defined syndrome or if a lesion can be demonstrated, the symptoms are accepted as organic. However, if the patient manifests signs of increased emotional tension or if the symptoms and signs are "atypical" or inconsistent or do not follow well known organic patterns, they are often considered psychogenic. Sometimes there is a combination of the two types.

In either instance the symptoms are due to a disorder in function. The patient's reactions in the case of an organic disorder are just as functional as in the case of a neurosis. The difference between the two lies in the origin of the functional disorder and in the manner in which the symptoms manifest themselves. Nevertheless, close analysis will reveal that in many instances apparent hysterical reactions follow consistent and specific physiologic patterns, and in such cases it may be difficult to differentiate the organic from the psychogenic syndrome.

In the course of an investigation of perceptual changes in a large group of patients with battle injuries of the brain, visual disturbances were noted in a considerable number of cases.[1] In 1 case a so-called ring scotoma, combined with an occasional tendency toward concentric contraction of the monocular and binocular fields, was discovered.

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1. (*a*) Bender, M. B., and Furlow, L. T.: Phenomenon of Visual Extinction in Homonymous Fields and Psychologic Principles Involved, Arch. Neurol. & Psychiat. **53**:29-33 (Jan.) 1945. (*b*) Bender, M. B., and Teuber, H. L.: Phenomena of Fluctuation, Extinction and Completion Associated with Visual Perception, ibid. **55**:627-658 (June) 1946; (*c*) Nystagmoid Movements and Visual Perception: Their Interrelation in Monocular Diplopia, ibid, **55**:511-529 (May) 1946.

Such visual disturbances have been considered by many authorities as psychogenic, even in cases of head injury, if pathologic changes in the retina itself could not be demonstrated.[2] Evidently, this functional interpretation was prompted by the fact that these field defects could not be explained on a neurophysiologic basis. But, for the same reason, this class of changes, comprising contracted fields, shifting fields, fields with spiral contour and ring scotomas, has become a domain of unlimited debate in the literature. Some of the reported observations and interpretations on this subject are reviewed in the following section.

PREVIOUS OBSERVATIONS

Tubular Fields.—Concentrically contracted fields were originally interpreted as arising always from actual disease of the peripheral organ. Von Graefe,[3] in 1865, conceived of *anaesthesia retinae,* which appeared on perimetric examination as absolute blindness in the periphery of the field. Although he recognized hysteria as the principal causative factor, he insisted on localization of the "disease" to peripheral zones of the retina, mainly because he was able to produce pressure phosphenes in the presumably blind regions of the field. Since these phosphenes arise directly in the optic nerve, he concluded that the anesthesia must be in the retina.

It was soon pointed out that hysterical fields were often characterized by inconsistency from one examination to another and by sudden, and yet frequently transitory, improvements. Moreover, patients with concentrically contracted fields were, nevertheless, in most instances well

2. On theoretic grounds, there is an obvious reason for grouping ring scotomas with other unusual field defects, such as shifting and spiral fields and concentrically contracted, or "tubular," fields, and for declaring all these changes to be psychogenic. The common denominator of all these fields is found in the fact that none of them can be interpreted in terms of accepted ideas of cortical representation of visual function. The usual field defects produced by focal injury to the brain correspond closely in shape, extent and location to the shape, extent and location of the injury to the optic pathway or radiation. Ring scotomas and contracted fields, on the other hand, obviously are not produced by ring-shaped or concentric lesions in the visual substrate. If their "organic" causation could be accepted in certain cases, they would seem to negate the wealth of evidence which has been accumulated, particularly since World War I, in favor of a topologic representation of the retina on a "cortical retina" (Klüver, H.: Visual Disturbances After Cerebral Lesions, Psychol. Bull. **24**:316-358 [June] 1927). However, there are serious doubts whether the evidence for topologic representation should necessarily be interpreted as point for point correspondence in a functional sense. More recently, departures from point for point correspondence, even in cases of clear-cut "organic" hemianopsias and quadrantanopsias, have been demonstrated.[1b]

3. von Graefe, A.: Vortäge aus der v. Graefeschen Klinik, zusammengestellt und mitgetheilt von Dr. Engelhardt, Klin. Monatsbl. f. Augenh., 1865, p. 265.

oriented in space and quite adequately avoided obstacles and moving objects in their peripheral fields. Their contracted fields seemed to exist primarily during perimetric measurement. Wilbrand and Saenger [4] therefore assumed that the constriction was produced by a temporary central depression of visual activity, viz., a corticofugal inhibitory influence on the processes of assimilation in the periphery of the retina. To indicate the fleeting character of many of these disturbances, they introduced the term "central fatigue." Von Bechterew,[5] however, again (in 1894) made the assumption that there was hypesthesia of the retina, produced by local anemia of its peripheral zones.

In the same year, Janet [6] formulated the strictest "functional," and hence central, interpretation of these phenomena. For him, tubular fields were the hysterical symptom *par excellence*. They inform the examiner of the patient's basic weakness of self perception, which, in turn, leads to an inability to relate impressions to the perceiving self. While this theory might be given a truly physiologic meaning, it was widely interpreted as though some form of weakened attention were responsible for the contraction of the fields of vision. In order to disprove such theories of attention Klien,[7] in 1907, compared the perimetric fields obtained from frankly psychotic patients, deteriorated epileptic patients and delirious alcoholic persons, on the one hand, with tubular fields of hysteria, on the other. The outlines of the fields of the psychotic subjects—presumably influenced by fleeting attention—were found to be characteristically "jagged," while the fields of hysterical patients always showed a smooth, concentric contraction. Klien's own attempt to explain such tubular fields was virtually in terms of simulation; he stated, in effect, that the hysterical person is imbued with the general idea, "I am ill"; during perimetric examination this preoccupation manifests itself as "I can't see."

After the gamut of theories of causation, ranging from peripheral to central, and from metabolic disturbance to simulation, had been exhausted, World War I brought cases which to Goldstein [8] seemed to show without doubt that tubular fields could be the direct result of

4. Wilbrand, H., and Saenger, A.: Ueber Sehstörungen bei funktionellen Nervenleiden, Leipzig, F. C. W. Vogel, 1892.

5. von Bechterew, W.: Ueber die Wechselbeziehung zwischen der gewöhnlichen und sensoriellen Anästhesie, Neurol. Centralbl. **13**:252-297, 1894.

6. Janet, P.: État mental des hystériques, Paris, Rueff & Cie, 1894.

7. Klien, H.: Ueber die psychisch bedingten Einengungen des Gesichtsfeldes, Arch. f. Psychiat. **42**:359-450, 1907.

8. (*a*) Goldstein, K.: Die Lokalisation in der Grosshirnrinde, in Bethe, A.; von Bergman, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1927, vol. 10, p. 600; (*b*) Constriction of Visual Fields, Arch. Neurol. & Psychiat. **50**:486-487 (Oct.) 1943.

well defined lesions (gunshot wounds) of the brain, particularly the occipital lobes. He also made an observation of considerable practical importance: Concentric contraction of truly "organic" origin may be found with the tangent screen but not on perimetric examination. The physiologic basis of these phenomena was tentatively described by Goldstein as an abnormal fatigability of the central visual substrate. According to him, the reduced excitability of the visual substrate is generalized, involving the entire occipital cortex, and even other parts of the brain. He stressed that the concentric contraction is not due to a topologically corresponding lesion. Because of the normal physiologic inferiority of the more peripheral parts of the field of vision, he stated that the periphery is hardest hit during a general depression of visual function, thus yielding a tubular field.

Shifting and Spiral Fields.—In plotting tubular fields, Förster discovered (according to König [9]) that the field was always smaller when the centrifugal motion of the target along any meridian was reversed and the target moved across the center and back toward the periphery. This shifting of the boundaries of the visual field (Förster's shift type) was considered as a means of differentiating "genuine traumatic neurosis" from malingering. It was attributed sometimes to retinal, sometimes to central, fatigue. However, it soon became evident that a similar shifting could be obtained with this form of perimetry for normal fields, although the extent of the difference between the boundaries obtained on centripetal and on centrifugal motion of the target was much less pronounced than with pathologic fields. The shifting itself seemed clearly related to the difference in threshold values found in any experimentation on psychophysical thresholds. Thus, there is always a discrepancy between measurements taken with an ascending series of intensities, which somewhere cross the visual threshold, and results obtained from a descending series, which starts above the threshold and is gradually made to fall below it. However, the exaggerated shifting in pathologic fields seemed to require an explanation. In the literature, this was attempted on the basis of two factors: inattention (fluctuation of the attention [9]) and retinal fatigue.[4] Inattention can be excluded on the basis of Klien's results.[7] For shifting fields the theory of fatigue seems comparatively more appropriate because in many cases it may be found that the effects which lead to the "shifting" in the field of vision become cumulative—a characteristic of physiologic fatigue. That is, every time the target is reversed and directed toward the periphery on the opposite side, it disappears there

9. König, O.: Ein objectives Krankheitszeichen der traumatischen Neurose, Berl. klin. Wchnschr. **28**:774-778. 1891.

sooner, or at a point which is a few degrees closer to the center. If meridian after meridian is thus tested, the contraction will appear to increase continually, and the total outline of the field will present the picture of an "exhaustion curve" (Wilbrand and Saenger), frequently a spiral.

Ring Scotomas.—It was Goldstein [10] who first pointed out that the obscure phenomenon of ring scotoma may be closely related to that of oscillating (shifting) fields and to concentrically contracted fields, as found in patients with organic disease. With the collaboration of the psychologist Gelb, he analyzed 6 cases of ring scotoma in battle casualties of World War I. In contrast to all previous investigators, who attributed ring scotomas either to hysteria or to specific lesions of the retina, Goldstein assumed a central causation. Although he couched his explanation in terms of cortical "fatigue," it is evident from his case reports that fatigue in his sense is directly related to mode, intensity and duration of excitation in the visual organ. He observed that with slow inward motion along every meridian a target disappears after it has reached a certain zone (Goldstein found on the average a zone extending 60 to 40 degrees from the center). This he explained in terms of "fatigue." However, with continued centrifugal motion the greater excitability of the central region of the field comes into play and the target becomes visible again, thus yielding a ring scotoma. Investigation during the period between the two wars apparently did not continue along the lines suggested by the approach of Goldstein and Gelb. From the inclusive review of literature by Strauss and Savitsky on head injuries, in 1934,[11] it appears as though ring scotomas in cases of injury to the brain were still attributed rather dogmatically to hysteria, or to such conditions as concurrent commotio retinae.[12]

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10. (*a*) Gelb, A., and Goldstein, K.: Ueber Gesichtsfeldbefunde bei abnormer "Ermüdbarkeit" des Auges (sog. "Ringskotome"), Arch. f. Ophth. **109**:387-403, 1922. (*b*) Goldstein, K.: After-Effects of Brain Injuries in War, New York, Grune & Stratton, Inc., 1942; (*c*) footnote 8 *a*.

11. Strauss, I., and Savitsky, N.: Head Injury: Neurologic and Psychiatric Aspects, Arch. Neurol. & Psychiat. **31**:893-955 (May) 1934.

12. This was done in spite of the rarity of clearcut ring scotomas, even in cases of disease processes localized to the retina and the optic nerve. Thus, Nicoletti (Sul comportamento e significato clinico della scotoma anulare nelle affezioni delle membrane interne dell'occhio e del nervo ottico, Ann. di ottal. e clin. ocul. **54**:879-924, 1926) found only 33 instances of ring scotoma among 10,000 cases of disease of the eye and classified the defect as due to retinitis pigmentosa, syphilitic chorioretinitis, myopia, injury to the eye, glaucoma and optic neuritis. Langdon (Ring Scotoma, in Contributions to Ophthalmic Science, Dedicated to Dr. Edward Jackson, in Honor of His Seventieth Birthday, March 30, 1926, Menasha, Wis., George Banta Publishing Company, 1926, p. 274) added

Strauss and Savitsky reported 2 cases of their own, which are of interest because the ring scotomas (unilateral in the first case and bilateral in the other) were found only on the tangent screen. Although the symptoms followed severe trauma to the head in each case, the authors were inclined to assume the existence of a "functional factor" for at least 1 of their cases. On retesting the fields of their patients two to four weeks after the original tangent screen studies had been made, they found that the unilateral scotoma in the first case "was beginning to break up into islets of absence of vision." In the second case the fields appeared greatly contracted bilaterally: "The narrowing of the fields was so marked that it overlapped the site of the annular scotomas." Evidentally, on reexamination the ring scotoma had been replaced by a tubular field.

In view of the fact that the majority of the authors have regarded ring scotomas and tubular and spiral fields as psychogenic, we endeavored to investigate the nature of the complex functional disorder by subjecting our patient to a series of special examinations. In our group of patients with injuries of the brain, it was noted that the introduction of psychophysiologic procedures often made it possible to understand even seem-

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commotio retinae, migraine, disease of the nasal sinuses and solar retinitis as causative factors. Ring scotomas attributed to hysteria were reported earlier by Wölfflin (Ueber ein seltenes Gesichtsfeldsymptom bei Hysterie, Arch. f. Augenh. **65**:309-312, 1910) and de Schweinitz (The Relation of the Visual Fields to the Investigation of Certain Psychoses and Neuroses, Univ. Pennsylvania M. Bull. **22**:282-294 [Dec.] 1910), cited by Strauss and Savitsky.[11] Loddoni (Sur un cas de scotome annulaire par la quinine, Ann. d'ocul. **166**:733-742, 1929) described a case of ring scotoma following quinine poisoning, and LeBlond (Un cas de scotome annulaire bilatéral d'origine traumatique, Ann. d'ocul. **161**:740-741, 1924) reported cases of bilateral ring scotomas following head injury. Only comparatively few case reports have been added during the last ten years. Macular burning was recently shown to be responsible for ring scotoma (Loewenstein, A., and Steel, J.: Macular Burning and Ring Scotoma, Glasgow M. J. **135**: 73-85 [March] 1941). Krimsky (Symmetric Incomplete Annular Scotoma of Tobacco Origin Without Enlargement of Blind Spot, Am. J. Ophth. **17**:722-725 [Aug.] 1934) reported a case of ring scotoma associated with tobacco amblyopia. Other cases were recorded by Borsello (Ring Scotoma in Disturbances of Optic Nerve Due to Arachnoiditis, Rassegna ital. d'ottal. **9**:101-137 [Jan.-Feb.] 1940), in which the scotoma resulted from arachnoiditis; by Meyerbach and Loewenberg (Bilateral Ring Scotoma of Five Years' Duration, Arch. Ophth. **22**:674-678 [Oct.] 1939) (in which the cause was undetermined), and by Callahan (Annular Scotoma, Am. J. Ophth. **24**:196-199 [Feb.] 1945). Lillie and Adson (Unilateral Central and Annular Scotoma Produced by Callus from Fracture Extending into Optic Canal: Two Cases, Arch. Ophth. **12**:500-508 [Oct.] 1934; Tr. Sect. Ophth., A. M. A., 1934, pp. 90-99) described 2 cases of unilateral central and annular scotoma due to callus from fracture extending into the optic canal.

ingly bizarre complaints.[13] The pathologic modifications in visual function were therefore studied by a combination of available clinical methods and technics of the psychologic laboratory. Perimetry and tangent screen tests were thus supplemented with tachistoscopic examinations and with studies of after-imagery, perception of movement, color, depth and apparent size. Various tests of relative and absolute localization in visual space were made. Thresholds for fusion of flicker were computed for different degrees of eccentricity from the macula. In addition, the patient's reports were recorded verbatim and drawings obtained whenever possible (this qualitative material could be used rather safely in cases in which the damage to the brain was limited and in which the possibility of simulation and of gross forms of hysteria had been excluded). In the case reported here this triad of neurologic, psychophysiologic and "phenomenologic" methods was applied throughout.

REPORT OF A CASE

A water tender third class, aged 28, sustained multiple injuries from shrapnel and concussion, on Oct. 25, 1944, while he was engaged in fighting fires within a closed compartment of his ship. He was stunned but presumably not unconscious. There was immediately a deafening ringing in his right ear, but he did not notice any phosphenes or other visual disturbances. Although his left hand seemed to him "stiff" and unmanageable, he was able to use all extremities in going over the side of his own vessel and in climbing over a cargo net aboard another ship which was standing by. There it was found that he had wounds in his right arm, his right thigh and leg and the lower part of his left leg. The left ear drum was red and torn, and the ear was draining. This discharge stopped spontaneously twelve days after the injury. Above the ear, in the right temporal region, there was a scalp wound, which (two months later) proved to be a compound fracture of the skull, close to the midpoint of the temporoparietal suture.

For the first two months after the injury treatment was concentrated on the patient's leg wounds, which ran an irregular septic course. Repeated surgical intervention was necessary for the removal of foreign bodies from the right thigh. The existence of an intracranial injury was established, when the patient's complaints of severe temporofrontal headaches and difficulties (pain) in closing his jaw persisted, even after the small wound in the scalp above the right ear had healed. Roentgenographic studies on Dec. 18, 1944 showed evidence of depression of the fracture near the temporoparietal suture and some indriven fragments of bone, but no foreign body. A radiolucent shadow anterior to the coronal suture in the right lateral view suggested originally (on December 18) an

13. Psychophysiologic methods require such strict internal consistency of the patient's reports that simulation or crude forms of hysteria could soon be recognized as such. Nevertheless, patients with presumably psychogenic complications were not simply dropped from the series but were studied in exactly the same fashion as those with "purely organic" conditions. This was done in the hope of determining the extent of similarity or dissimilarity which may exist between the visual disturbances in the so-called post-traumatic neuroses and those visual difficulties which result directly from cerebral trauma.

additional fracture of the skull just above the right orbit. However, on repeated roentgenographic examinations (up to Sept. 19, 1945) the latter area of diminished density could not be definitely identified (fig. 1).

On Jan. 4, 1945 a decompression of the skull fracture was performed. Since the patient continued to complain of pain in the head and the right side of the face, even after the decompression, further studies to determine the cause of the pain were made. Roentgenograms of the maxilla, zygoma and paranasal sinuses revealed no abnormalities. There was no clinical evidence of sinusitis.

Further neurosurgical intervention was not indicated, since neurologic examination on January 30 showed an essentially normal status except for homonymous defects in the visual fields on the left, defective hearing in the right ear [14] and diminished pain sensation over the left side of the body. The last defect, however, could be demonstrated only on application of simultaneous double stimulation to

Fig. 1.—Roentgenogram of the skull, revealing an old defect in the right temporoparietal region.

corresponding parts of the right and the left half of the body.[15] The facial pain was finally considered to be due to a disorder in the function of the temporomandibular joint.

This pain, together with recurrent headaches, some dimming of vision and pronounced loss of hearing in the right ear, continued to be the patient's outstanding complaints. These symptoms were unchanged when he was seen again, one month after his discharge from the service.

PSYCHOMETRIC AND PERSONALITY STUDIES

Special psychometric and personality studies were made on Feb. 5, 1945 by Lieut. (jg) J. W. Diamond. She reported the following results: On the

14. On the audiogram, the hearing loss in the right ear amounted to 20 to 30 decibels for the lower frequencies, with a drop to 50 decibels in the highest range of frequencies. The fundi were normal, and the patient showed no signs of myopia.

15. Bender, M. B.: Extinction and Precipitation of Cutaneous Sensations, Arch. Neurol. & Psychiat. **54**:1-9 (July) 1945.

Wechsler-Bellevue adult intelligence scale the verbal intelligence quotient was 111, the performance intelligence quotient 98 and the full scale intelligence quotient 105. The intellectual level was average. No difficulty in calculation existed. Memory for repeating digits forward was found to be superior (eight digits), but when the patient was asked to reverse the order he was unable to go beyond a series of four. With performance items, the patient did not do as well as on the verbal scale, but his ability in reproducing block designs and in assembling objects was on his average level. The Benton visual retention test[16] revealed no deficiency (the patient reproduced correctly 7 designs out of a total of 7). The Shipley Hartford scale gave him a superior vocabulary but only dull normal thinking ability, "with a conceptual quotient indicative of intellectual impairment." On the Hunt-Minnesota test for organic damage to the brain, the discrepancy between expected score and actual score in learning paired words and paired designs was "extreme, and suggestive of diffuse organic disease of the brain (T score 82)." The Rorschach record, finally, was considered to be within normal limits, with none of the signs which are presumably pathognomonic of severe organic (post-traumatic) change. The only deviant trend was a tendency to pick out unusually minute details for interpretation, which, it was felt, reflected "an obsessiveness or meticulousness of personality."

Six months later, when he was retested with some of the tests which had yielded results outside of "normal" limits on the first trial, it was found that there was no longer any discrepancy between the expected score and the obtained score in the Hunt test. Retesting with specific subtests of the Wechsler-Bellevue scale indicated that all intellectual abilities were now on a fairly even average level, without any significant disparities. The psychologist noted, however, that the patient, though cooperative, was rather tense throughout the testing procedure. "He manifested a rigid, inflexible approach to the various tasks set before him and became upset with any feeling of pressure or with any hint of failure. It was noted that he either performed very efficiently or became totally lost and unable to function at all: For instance, he would learn the paired words well, then make one error and become completely confused. His general attitude was uncompromising and perfectionistic, and he showed unusual extremes in efficiency, which depended not on the type of the mental tasks but, apparently, on the feeling of pressure or impending failure." These psychologic reports are of interest, even though their evidence for an original mild post-traumatic change in personality may not be conclusive. They characterize in a clinical fashion the patient's personal "style" of functioning, which he exhibited throughout the numerous subsequent tests of his visual perceptions.

AWARENESS OF VISUAL DEFECT

The patient's spontaneous complaints about his vision were considerably less frequent than those about his infected leg wound, his hearing difficulties and his persistent headaches. All that he would say was that his vision was "dimmed" and that his eyes were readily tired and "watered" more than usual. When asked to specify his descriptions, he made the following statements: 1. Ever since his injury both eyes had seemed to be covered with a film or haze. This film was transparent and of seemingly equal density for the two eyes. If he closed either eye, the film appeared thicker (less transparent). It always seemed to cover

16. Benton, A. L.: A Visual Retention Test for Clinical Use, Arch. Neurol. & Psychiat. **54**:212-216 (Sept.) 1945.

the whole eye evenly. 2. About six months after the injury he began to be less aware of this film, noticing it only after straining his eyes, as in reading. Then the blurring of images would bring the film back to his attention. 3. He also noted at this time that the film seemed to fluctuate in density. With prolonged fixation on any one object, it became thicker and momentarily obscured either part or all of the objects within his field of vision. He would then close his eyes and wait for a few seconds, and after this his vision seemed to have recovered, until the cycle started anew. 4. Whenever he closed his eyes under these conditions, the film was not immediately abolished but appeared broken up into brightly luminous dots—"a film of snowflakes." These crystal-like phosphenes covered the whole field evenly. As time went on, the patient noticed these phenomena less and less, and in September 1945 they had almost disappeared. 5. In addition to these diffuse changes in vision, the patient became aware, shortly after his injury, of a definite "blank spot" localized to the left corner of the left eye. This spot impressed him neither as darkness nor as a film or haze; "things simply weren't there." By June 1945, or eight months after the injury, this feeling also had been "eliminated" as the patient put it. 6. Even a year after the injury the patient found it impossible to drive a car unassisted. As his main difficulty in this respect, he described a peculiar "jumping" of the roadside at his left, particularly on driving through a curve. "The side of the road suddenly jumps out [from the left] into the middle of the road—as if I were driving suddenly beside the road, instead of driving on it."[17] 7. He also complained of rapid ocular fatigue, noted when he was trying to read more than a few paragraphs or when he was watching a movie for more than a few minutes. "Things dim out still and then come back again."

In order to evaluate the patient's complaints, numerous clinical and psychophysiologic tests were made over a period of eight months (January to October 1945). All these tests were administered under standard conditions, that is, in exactly the same way as for other patients in our series with head injury, as well as for a group of normal subjects.

PERIMETRIC EXAMINATIONS

Perimetric studies with an illumination of 1 foot candle, a distance of 33 cm. and 1 degree targets (white and red) revealed consistently on different dates (Feb. 12 to Aug. 13, 1945) an absolute scotoma (semicrescent) in the periphery of the left lower temporal quadrant, reaching to within 60 degrees of the point of fixation (fig. 2). The density and extent of the scotoma remained unchanged from one examination to another. Significant contractions of the fields for red were not elicited at any time.

TANGENT SCREEN STUDIES

While the results of routine perimetric examinations were consistent and remarkably unchanged from one examination to another, the use of the Bjerrum

17. The patient's description of these sudden displacements in visual space closely resembles a phenomenon which is obtained by normal subjects on observing the rapid passing of a visual stimulus (light or illuminated slit) through the aperture in a screen. Under these conditions, the stimulus object "jumps" into the field; i. e., it is already considerably past the edge of the diaphragm when it is first perceived (Fröhlich phenomenon [Fröhlich, F. W.: Die Empfindungszeit, Jena, Gustav Fischer, 1929, p. 365]).

screen led to a seemingly confusing array of results. The readings changed as time went on, but they also differed on any single day with different methods of examination.

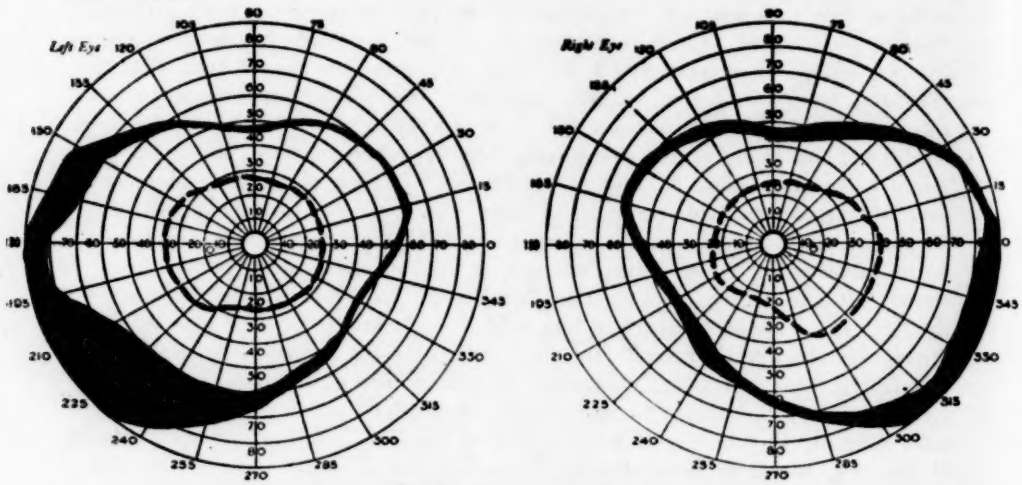

Fig. 2.—Perimetric charts, illustrating crescent defect in the left lower temporal field of vision. Solid black indicates an absolute scotoma for no. 1 degree target at a distance of 33 cm. and with 7 foot candle illumination. Lines of dashes represent boundaries of the color field for red plotted under the same conditions.

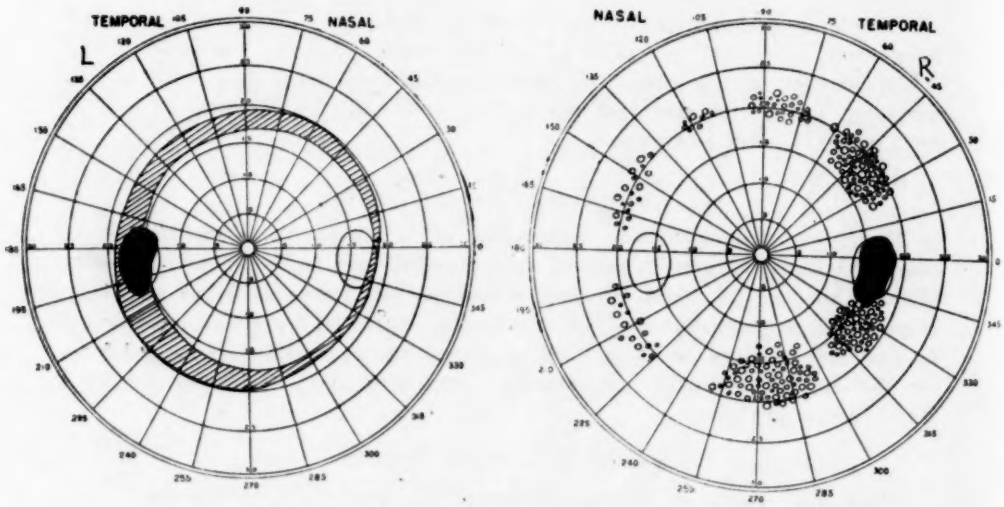

Fig. 3.—Tangent screen field charts, illustrating a relative ring scotoma in the left eye and an incomplete ring scotoma in the right eye. Solid black represents the physiologic blindspot. Diagonal lines in the left eye indicate the region in which a 2 mm. target at a distance of 1 meter disappeared. Small circles in the right eye designate islets of impaired vision. See text for details. Note that the annular scotoma is more pronounced in the eye opposite the cerebral lesion.

On Feb. 13 and Feb. 20, 1945, central fields were taken on a Bjerrum screen with a 2 mm. target. The patient was seated 1 meter from the fixation point. The targets were brought in (from 30 degrees to the fixation point) with slow, steady,

centripetal motion along each half-meridian. When the left eye was tested under these conditions, the target disappeared within an annular zone in the field of vision (fig. 3). This zone occupied a region between 15 and 20 degrees of the fixation point. The heaviest portion was always found on the temporal side of each eye. If a larger target was used or if the patient's distance from the screen decreased, the "ring" sometimes became incomplete on the nasal side. Likewise, a different field resulted with rapid centripetal motion of the target; under these conditions the "ring" was found as much as 5 degrees closer to the center, or it was not found at all. With centrifugal motion of the target, the "ring" was usually not encountered until the target had been moved beyond 20 to 25 degrees from the center. Actually, then, the zone of disappearance no

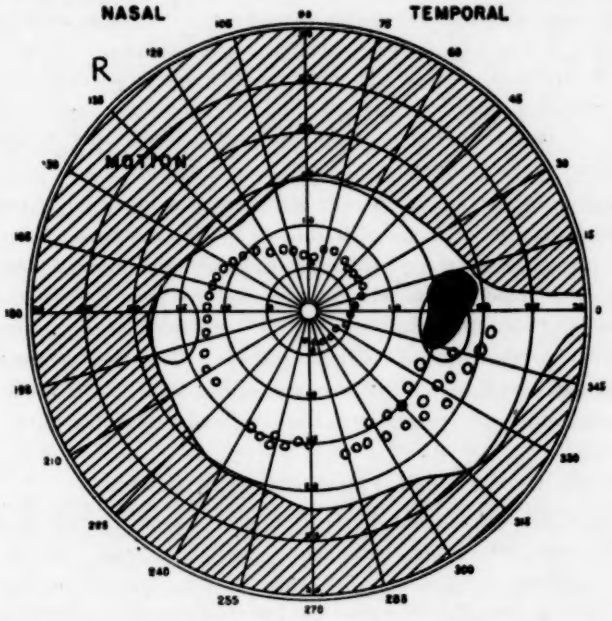

Fig. 4.—Chart of the central field of the right eye, plotted on the tangent screen. A 2 mm. target at a distance of 1 meter was moved slowly inward from the periphery toward the fixation point. The test was started at the zero (right horizontal) meridian and repeated for each meridian in a clockwise succession. This yielded a contracted, or tubular, field for form and color but not for motion. The boundary of the field is defined by the diagonal lines. The small circles represent zones of impaired vision. Note the spiral shape. The field for the left eye was similar to that for the right eye except that it was more contracted.

longer represented an annular scotoma. In most instances the target did not reappear with continued outward motion once it had become invisible, between 25 to 30 degrees from the center. The apparent ring scotoma had thus changed into a tubular field.

When the right eye was tested with the same series of varied conditions, corresponding results were obtained. However, a definite (continuous) ring zone of amaurosis was never established. Instead, numerous small "islands" of relative loss of vision were found between 15 and 25 degrees from the fixation point. In these areas the target was indistinct and colorless, fluctuated in visibility or

became entirely extinct (fig. 3). In comparing the fields of the two eyes, it was apparent that the annular defect was more complete in the field contralateral to the lesion. A similar difference between the two eyes had already been noted on perimetric examination.

With further tangent screen studies, it was found that when the direction of the moving target was reversed (outward) a transition into a kind of tubular field appeared in the right eye, just as it had been noted for the left eye. A particularly unusual picture (a type of spiral field) resulted whenever the 2 mm. target was led very slowly centripetally along each half-meridian in a clockwise order, starting from the zero meridian (fig. 4). Under these conditions, the targets appeared later and later during each test, or, to put it differently, the plotted field seemed to contract more and more as the examinations progressed. However, the target became immediately visible anywhere within the area of apparently reduced vision if it was moved more rapidly or was repeatedly shaken. In addition to this spiral contraction, a spiral zone of fluctuation and extinction was encountered. Along any meridian, after the target had first become visible, there was a tendency for the target to dim or fade out once again as the centripetal motion of the test object was continued.

Examinations repeated over a period of ten months yielded practically identical results, provided that the methods of testing were kept the same. The only change noted was a breaking up of the apparent ring scotoma into islands of impaired vision. This was found in the left eye two months after the ring scotoma was first discovered. From this time on the fields obtained on examining the left eye were similar to those found in the right eye. The ring scotoma in the left eye was no longer complete. There was an annular zone of "islands" of impaired vision (characterized by fluctuation and transient extinction of images) in each eye.

DEPARTURES FROM GEOMETRIC OPTICS

Examinations with the tangent screen thus gave a complex and variable picture. Sometimes concentrically contracted fields, similar to the "tubular vision" of the hysterical patient, were found. In view of this, special studies were made in order to check on the consistency of the patient's reports. Should his responses prove to be consistent, the same studies would be extended to investigate what influence these particular field changes had on his visual perceptions.

First of all, the patient's distance from the tangent screen on which the field tests had been made was systematically varied. Increase in distance from the screen obviously entails a proportionate increase in the linear projection of the visual angle. Thus, a contracted field of genuinely organic origin should show an apparent widening with increase in distance. Under the same conditions, a tubular field produced by hysteria or simulation either remains unchanged in its apparent diameter (absolute width on the screen) or varies in random fashion. With our patient, increase in the distance from the screen led pari passu to an (apparent) widening of the diameter of the ring-shaped "scotoma." However, this widening was found on repeated measurements to fall somewhat short of that required by geometric optics. Instead of subtending a constant visual angle, the ring became increasingly broad, and at the same time its diameter was somewhat shortened (relative to the visual angle) whenever the patient moved away from the screen. The same relationships held for conditions under which a concentric contraction or tubular field was obtained instead of (or in addition to) the apparent ring

scotoma. In relative terms, the fields were found to be shrinking, rather than remaining constant, with increase in distance. However, the extent of the shrinking did not approach the tubular contraction of the hysterical subject, who claims that his field is just as small at short distances as it is at long distances.

AUBERT–FÖRSTER PHENOMENON

It will be remembered that in spite of repeated examinations neither ring scotoma nor concentric contraction could be found in this patient on standard perimetric studies. These field changes could be demonstrated only with the tangent screen method. Earlier, Goldstein [8b] had pointed out that contracted fields of "organic" origin were often characterized by just this peculiar discrepancy. The main difference between the tangent screen method and perimetry in the plotting of fields lies obviously in the fact that with increasing distance from a point of fixation a target on the screen is also increasing its distance from the patient's eye.

There is experimental evidence [18] that the acuity of peripheral portions of a normal field of vision diminishes with increasing distances of the objects viewed. Thus, when a test object situated 15 degrees from a point of fixation is resolved at 1 meter, it may not be resolved at a distance of 2 meters and an eccentricity of 15 degrees even though the linear dimensions of the test object have been increased in geometric proportion. This effect is known in the literature as the Aubert-Förster phenomenon. Like the phenomena of size constancy,[19] this peculiarity of the periphery of the visual system constitutes a departure from the behavior which one would expect on the basis of strict geometric optics.

In our series of cases, the Aubert-Förster phenomenon was routinely studied under the following conditions: The patient was first seated at a distance of 150 cm. from a tangent screen. While he maintained binocular fixation on the center of two concentric circles (diameters, 13 and 26 cm., respectively), his peripheral acuity was examined. This was done either by means of Snellen's test types or by means of two white cards bearing one or two dark test lines. Each of the test lines was 2 cm. long and 2 mm. wide. On the card bearing two parallel test lines, the lines were 5 mm. apart. These cards were introduced from the periphery with moderately slow centripetal motion along each meridian. In at least three successive trials the point at which the patient was able to resolve the double line was ascertained. After all readings under these conditions ("large-far" constellation: 150 cm. distance, 2 cm. test lines) had been determined, the patient was moved to a distance of 75 cm. from the screen; the examinations were repeated with test cards bearing lines which were half as large ("small-near" constellation: test lines 1 cm. long, 1 mm. thick and 2.5 mm. apart) as those used at a distance of 150 cm. At the 150 cm. distance normal subjects usually managed to resolve the double line at about 10 degrees from the fixation point; at the 75 cm. distance the same subject resolved the double line at 13 to 15 degrees

18. (*a*) Aubert, H.: Physiologie der Netzhaut, Breslau, E. Morgenstern, 1865. (*b*) Jaensch, E. R.: Zur Analyse der Gesichtswahrnehmungen, Ztschr. f. Psychol. u. Physiol. d. Sinnesorg. (supp.) **4**:1-338, 1909. (*c*) Freeman, E.: Anomalies of Visual Acuity in Relation to Intensity of Illumination, Am. J. Psychol. **42**: 287-294, 1930.

19. Boring, E.: Sensation and Perception in the History of Experimental Psychology, New York, D. Appleton-Century Company, Inc., 1942.

from the fixation points. In other words, an Aubert-Förster phenomenon (or tendency toward concentric contraction of the functional field with increase in distance) can be noted for normal subjects under the conditions specified here.

As compared with the controls, our patient showed not only a pronounced reduction in peripheral acuity under all conditions but a disproportionate value for the Aubert-Förster phenomenon. With the "large-far" constellation he resolved the double line at 4 to 7 degrees, while with the "small-near" constellation he resolved the two lines at 8 to 10 degrees, from the fixation point. The inferiority of the "large-far" constellation as compared with the "small-near" constellation was evidently considerable. The results indicated that his fields were indeed contracted, but in a highly systematic fashion. Actually, it was not only a concentric contraction in the coronal (frontal-parallel) plane, but a drop in peripheral acuity in all three dimensions, thus producing a somewhat conical, or domelike, rather than a tubular (cylindric), contraction.

TACHISTOSCOPIC EXAMINATION

In all cases of our series, the various studies of visual fields were supplemented with tachistoscopic examinations. The latter tended to bring out minimal defects which could not be elicited by perimetric measurements or tangent screen tests. On the other hand, the tachistoscopic method sometimes revealed retention of visual function in areas in which perimetric studies indicated amaurosis.

Tachistoscopic examination of this patient elicited normal responses when he was confronted with a standard set of slides, exposed to either one or both eyes at a speed of 0.1 second or faster. There was neither the generalized slowing in recognition, sometimes found in cases of extensive damage to the brain,[8a] nor any significant tendency to miss large details in any region of the field up to 25 degrees from the point of fixation. In other words, the apparent ring scotoma and other discontinuities in the field as obtained on the tangent screen were not found on rapid (0.1 second) exposure. This is not surprising in view of the fact that in some instances the patient could see more on rapid than on prolonged exposure of a test object.[1b]

PROLONGED EXPOSURE OF SIMPLE STATIONARY PATTERNS

If the patient fixated an object for more than ten seconds, he reported dimming, fluctuation in distinctness and intensity, and occasionally total extinction of the image. This was particularly apparent with simple configurations which were large enough to involve pericentral regions. For instance, the patient drew what he saw at various stages while fixing at the center of two concentric circles on a screen situated 75 cm. from the eye. He reported that first the outer and then the inner circle disappeared within fifteen to twenty seconds of continued fixation. This obliteration occurred in a discontinuous and irregular fashion. It appeared as a "fragmentation" of the field of vision. This fragmentation was more evident when a peripheral target was added to the field at 25 degrees (just outside the annular zone of continual fluctuation) and the patient was instructed to focus his attention on this stationary peripheral target while maintaining fixation in the center (fig. 5 *C*). In these circumstances, the outer circle tended to split, first closest to the peripheral target, then rapidly in many other places. Subsequently, the peripheral target itself would disappear, and in extreme cases the

inner circle, and even the center of fixation, would temporarily "black out" (see patient's drawings, fig. 5 *C*₁ *to* *C*₃). If the patient was permitted to move his eyes or to close and reopen them, the complete image reappeared, but with continued

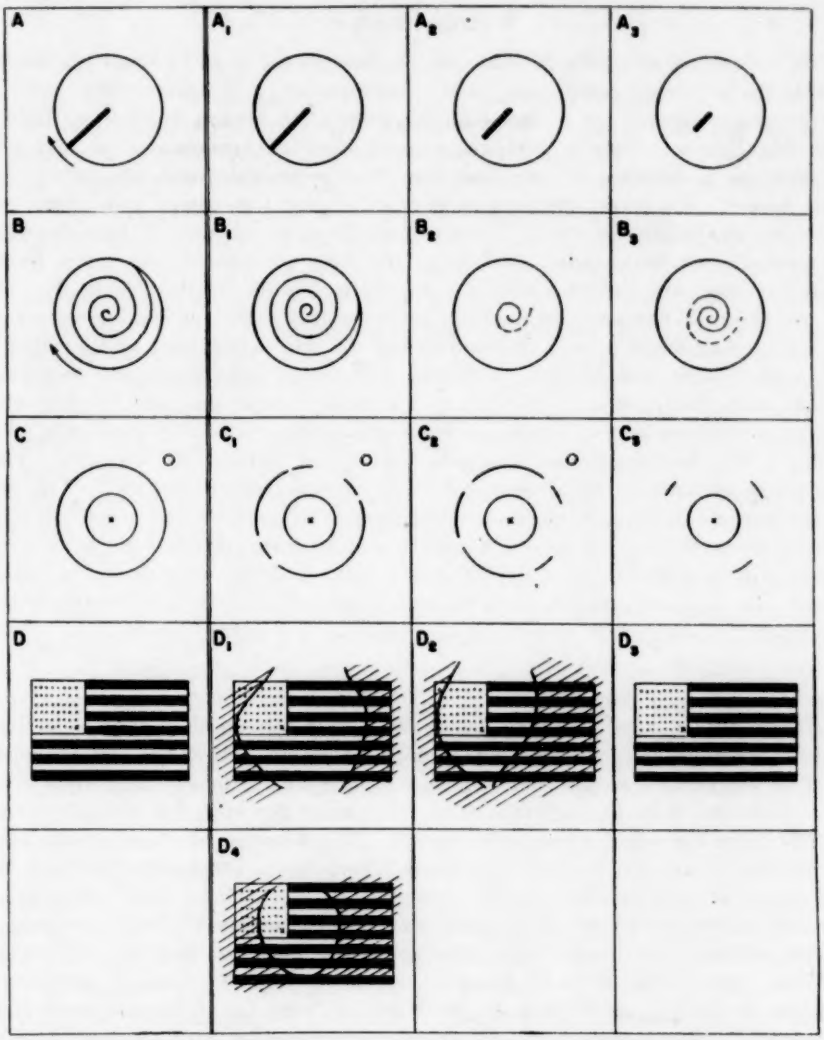

Fig. 5.—Various diagrams illustrating the concentric nature of the patient's visual defect. (*A*) The patient was shown a rotating Masson disk. A_1, A_2 and A_3 depict what he saw as rotations continued; the black line contracted successively toward the center whenever it swept through the left lower quadrant. (*B*) Rotating disk (plateau spiral) was shown the patient. What he saw is indicated by B_1, B_2 *and* B_3. Note the concentric shrinking of the spiral in B_2, interspersed with partial recovery (B_3). (*C*) The patient was instructed to fix at *X* and simultaneously attend to a target (small circle in the right upper quadrant). What the patient saw is indicated in C_1 to C_3. Note the fragmentation and resultant contraction of the image. In C_3 the peripheral target (small circle) has disappeared. (*D*) The American flag in complementary colors was used in tests of after-imagery. D_1 *to* D_4 represent a succession of phases of the negative after-image. Note again the gradual contraction of the after-image, interrupted by a phase in which the image was momentarily complete (D_3).

testing the periods of complete obliteration became longer and occurred more frequently. However, the recovery was always complete, at least momentarily, if the patient closed and reopened his eyes.

AFTER-IMAGERY

In a similar fashion, the patient's after-images tended to run through abnormally rapid cycles of disappearance and reappearance. Moreover, the patient's after-images decayed in a strangely irregular, but always concentric, fashion. He was able to obtain a strongly colored negative after-image on prolonged fixation on a drawing of the American flag printed in complementary colors (fig. 5 *D*).[20] However, the first appearance of the after-image took place only with an abnormally increased latency, regardless of whether it had developed monocularly or binocularly. Moreover, the first after-image was often incomplete; at times the patient reported a gap "1 inch wide" in the flag to the right of the point of fixation. In such an area the flag was invisible, or very faint and gray. Frequently only that portion of the flag which was to the right of the median plane was visible. When the after-image disappeared and then reappeared, only the portion to the left of the median plane was seen.[21] However, the most frequent course of the patient's after-images was as follows (fig. 5 D_1 to D_4): The first appearance was fully colored and more or less complete. Then the image disappeared and reappeared "with all four corners cut off." The next phase would often again be a complete image, followed by an image showing further obliteration of peripheral portions, and so forth, through ten to fourteen cycles within a minute or a minute and a half, until the after-image had faded away. In summary, visual after-imagery disclosed a concentric contraction of the field of vision, which seemed to take place as a continual process.

COLOR PERCEPTION

The patient's color sense, as tested with routine clinical methods (Ishihara plates; Jenning's wool skeins) appeared to be normal. However, on prolonged fixation on yellow, red or blue squares (5 by 5 cm.) exposed on a milk glass screen (40 cm. from the patient's eyes), the patient reported that the color faded rapidly from the edges toward the center. This decrease in chroma took place within the first twenty seconds of fixation. Sometimes, alternately the horizontal and then the vertical edges became colorless. The "fadings" were often interspersed with moments in which color was restored evenly to the whole square. If two squares of the same color were presented with time exposure (8 degrees to either side of the point of fixation), after the first few seconds, alternately the one on the left or the one on the right, or both, would become gray (i. e., colorless). After twenty to thirty seconds either one or both squares began to disappear and reappear in random fashion.

However, on tachistoscopic exposure of these colored squares, usually both squares were reported; the patient also reported positive after-images on these exposures. But either one or both of these squares tended to be colorless ("dark"), and this tendency increased with increasing speed of exposure. At a speed of

20. This test card measured 10 by 18 cm. It was placed in the frontal-parallel plane at the level of the patient's eyes, and fixation was maintained on the star in the lower right corner of the field of stars for thirty and/or sixty seconds at a distance of 30 cm.

21. These peculiarities of the patient's after-imagery were most pronounced on stimulation of the left eye. But they were also found on testing the right eye or both eyes under the same conditions.

0.01 second, when normal observers under our conditions had no difficulty in appreciating an intense single color, the patient saw only colorless (dark) squares, followed by two dark after-images, which faded almost immediately. These tests indicated a general, but slight, reduction in perception of color.

SPATIAL ASPECTS OF PERCEPTION

There were no gross disturbances in depth perception proper. Sizes and distances were gaged with practically normal accuracy. Evidently, the so-called perceptual constancies (constancy of size, shape and color) were not affected by the abnormality of the fields. However, objects moving in the periphery of his field frequently showed the peculiar "jumping" of which the patient had complained spontaneously. This, in a sense, could be called a disorganization of visual space, although it was most likely an expression of the abnormally pronounced fluctuation and extinction of images in the patient's periphery. (He would be aware of an incoming object for a moment; then it would become extinct and then reappear suddenly, after it had come closer to the center of the field.) Possibly, this particular difficulty was related to a disturbance in fixation which the patient showed, especially whenever he was asked to judge distances and sizes. He constantly turned his eyes and head to the left (i. e., in the direction of the principal scotoma). The occasional "jumpiness" even of stationary objects in the periphery might have been due to these ocular movements, which carried images of the objects alternately into and beyond the peripheral zone of decreased vision.

The patient's behavior in bisecting lines strongly pointed in the direction of an "organic" contraction of the field. He was instructed to attempt to bisect a line 15 cm. long at a distance of 30 cm. from his eye, with fixation maintained at one end. Regardless of the meridian in which the line was turned, the patient divided the line near the fixation point, making the peripheral portion too long. This occurred both with monocular and with binocular fixation. Indirectly, this was a manifestation of a concentric contraction of the field of vision, inasmuch as the peripheral portions of the lines seemed shorter to the patient than they actually were. When he was instructed to fixate the midportion of the line, he still erred considerably; but he then showed a consistent tendency to make the portion to his left too long. This was in keeping with the scotoma in his left temporal field of vision. In point of fact, a normal subject will (on monocular fixation) slightly overestimate the temporal portion of a given line if the line is oriented along the horizontal meridian. But this error in bisection of the normal subject rarely exceeds 0.3 per cent of the total length of the line.

With the stereoscope, the patient had the greatest difficulty in obtaining a Panum phenomenon.[22] The depth effect produced by horizontal disparity of two

22. Panum (Woodworth, R. S.: Experimental Psychology, New York, Henry Holt & Company, Inc., 1938) was the first to note that an impression of tridimensionality was obtained on exposing stereoscopically two pairs of parallel vertical lines, provided that the distance between one pair of lines was slightly in excess of the distance between the other. His observation became one of the crucial experiments for the classic theory of binocular depth perception (which assumes horizontal disparity of retinal points as the principal "clue" for depth). In the more recent work on perception of visual space (Werner, H.: Dynamics in Binocular Depth Perception, Psychological Monographs no. 218, Columbus, Ohio, Psychological Review Company, 1937, vol. 49, no. 2, p. 1), the Panum phenomenon is considered as only a special manifestation, but still illustrative of the general dynamics of binocular depth perception.

pairs of parallel vertical lines, where each pair is presented to one eye, was never observed. If two pairs of circles were substituted for the lines, a depth effect could be obtained, although it was transient and produced intense binocular rivalry. However, binocular rivalry was not the principal difficulty in his stereoscopic vision. If three letters (*X Y Z*) were presented in such a way that each letter had to be built from monoculaly presented half-images, a curious form of rivalry resulted which involved portions of the images of the letters to the right (*X*) and left (*Z*) but not the letter in the center (*Y*). The *X* as well as the *Z* appeared either distorted or incomplete; the *Y* appeared normal.

STROBOSCOPIC MOTION

A stroboscopic effect was produced as follows: On a vertical panel, a black disk rotated at variable speed. The speed was controlled by a rheostat, and the instrument was calibrated over a range of zero to 56 rotations per second.[23] On the black disk two white strips of paper were fastened, the larger one being nearer the periphery and the smaller strip diametrically opposite it and closer to the center. A gray screen was placed in front of the panel. In this screen two small apertures were cut (oblongs, 2 by 1 cm., one 3 cm. above the other) and placed in such manner that they would alternately expose portions of the white strips on the rotating disk. When the upper strip rotated through the upper window, the lower window was black; as the disk continued to turn, the upper window became black, and the lower window exposed the white strip. At low speed this succession was seen as such, i. e., as an alternation of black and white. With increase in speed a gray flash appeared, which seemed to move swiftly (with each half-turn of the disk) from window to window across the gray screen. At still higher speed the windows seemed to flash simultaneously, until each became a uniform dark gray. The screen was adjustable in such a manner that the apertures could be brought into any meridian of the patient's field. Furthermore, a movable fixation mark was provided, so that the windows could be observed by the patient at any desired degree of eccentricity.

In this particular case, observations could not be made at more than 10 degrees from the center because the patient was unable to resolve the two windows at greater distances from his point of fixation. The observations were complicated by a particularly rapid "dimming" and frequent temporary extinction in the tested zones of the field of vision. However, we could ascertain the following departures from the behavior of normal subjects on this test [24]:

(*a*) A lowered threshold for stroboscopic motion (appearance of the gray flash across the screen) occurred in central fixation and as far as 5 degrees from the center along each 45 degree meridian.

(*b*) At an eccentricity of 10 degrees along each 45 degree meridian in each quadrant, the patient did not obtain a clearcut stroboscopic effect. Instead, the impression of successive alternating flashes changed with increasing speed directly into the impression of simultaneous flicker. Under these conditions, normal observers showed a strong stroboscopic effect at such a degree of eccentricity.

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23. Lieut. Comdr. D. R. Sword, U. S. N., United States Naval Repair Base, San Diego, Calif., designed the multiple purpose instrument which was employed in these and in numerous other studies on perception of color and motion and supervised its construction and calibration.

24. Details and quantitative data, together with the standards derived from experimentation with normal controls, will be presented separately in a report on perception of motion in defective visual fields.

(*c*) If a stroboscopic effect in the periphery was obtained in the patient under these conditions, it tended to be partial or fragmentary. That is, only one of the windows jumped part of the distance toward the other, which flickered but remained stationary (singular motion); or both windows were seen by him as bouncing toward each other "as if they wanted to get together, but they snap apart before they meet" (dual motion).

(*d*) These fragmentary stroboscopic effects were noted only on increasing the speed to 2.6 rotations per second for the right upper quadrant of the binocular field of vision, which represents nearly one and one-half times the speed at which optimal motion could be obtained in the center (1.7 rotations per second). In order to obtain motion for the right lower quadrant, the speed of the apparatus had to be increased to 3.5 rotations per second, or to almost twice the speed necessary for the center.

(*e*) In the left half of the binocular field partial motion was obtained for the upper quadrant, but only occasionally, and not until the speed of 4.6 rotations per second had been reached. The left lower quadrant yielded motion with a speed of 9 rotations per second, that is, only after the state of simultaneous flashing (flicker) had been reached for all other quadrants, as well as for the center. The effect was transitory, and perhaps was nothing but the usual "bobbing" of peripheral objects which had always been noted, particularly in this quadrant. These tests showed that even the more central parts of the left lower quadrant were defective.

FLICKER AND FUSION

It was noted throughout our series of cases of cerebral injuries that one of the strictest tests of relative field defects is the evaluation of fusion frequencies of visual flicker in various parts of the field. Particularly in resolving hemianopsias, a lowering of the threshold at which an intermittent light stimulus appears to be steady (fused) may be the last sign of a field disturbance long after perimetric examination has failed to show any pathologic condition.

For this patient, flicker was produced by means of a small Masson disk[25] rotated on the panel used for the series of stroboscopic observations. The thresholds for fusion under these conditions proved difficult to determine, since the images tended to fluctuate spontaneously for the patient, so that he was at a loss to indicate at which moment the "actual" flicker had stopped. (*a*) There was an abnormal variability of threshold even on central fixation. (*b*) In spite of this, the threshold for fusion was clearly lowered for the center as compared with results obtained from normal observers under our conditions.[26] (*c*) As compared with the normal, the various quadrants showed further decreases in threshold values, with the greatest dip in the left lower quadrants, again demonstrating decrease in another type of visual function of the peripheral field.

TRUE MOTION

The patient had some difficulty in judging the relative and absolute speeds of objects, which may have been somewhat related to his difficulty in fixation and

25. A white disk with a single black line drawn from center to periphery, resembling the dial of a clock with a single hand.

26. Quantitative data, together with observations on normal controls, will be presented in a separate report on flicker and fusion in defective visual fields.

pursuit. (For normal observers, the phenomenal speed of a moving object tends to be higher when the object is regarded while it moves past a stationary point fixated by the subject; the speed appears to be lower if the subject follows the moving object with his gaze.)

However, the most outstanding disturbances were noted in this patient when continuous motion of an object involved large portions of his field of vision. A moving stimulus was again provided by a Masson disk. This disk was rotated relatively slowly (at speeds of from 1 to 3.5 rotations per second) while the patient maintained fixation on the center of the disk at a distance of 35 cm. under standard illumination. The patient soon became aware of a curious effect: The "hand of the clock" shrunk with each rotation, beginning at the periphery (fig. 5 *A*). This shrinking seemed to occur in a discontinuous fashion; whenever the black line swept through the left lower quadrant, it contracted a little farther. If the Masson disk was replaced with a rotating black spiral on a white ground (a stimulus used by us in the experimentation with motion after-images), the patient announced an analogous effect (fig. 5 *B*): The spiral seemed to shrink progressively as rotations continued.

COMMENT

At first glance, the results from this array of tests are so varied that one might be tempted to interpret the case as one of hysteria. An additional basis for such a suspicion is the persistence of the visual disturbances as such.[27] On the other hand there was nothing in the man's previous history or in his behavior during the period of observation to suggest a hysterical disorder. Special personality studies did not reveal significant neurotic reactions.

Moreover, there were several organic features in this man's illness, such as (*a*) a penetrating wound of the skull, (*b*) a temporal crescent defect in the field of vision in the contralateral eye and (*c*) consistency of his responses whenever he was subjected to the same test on various occasions. However, it was pointed out that on different tests his responses were discrepant and at times atypical. The most apparent of these seemingly contradictory observations were the following: (1) the discrepancy between the fields as determined with the perimeter and with the tangent screen; (2) fluctuations in visibility of the targets on different examinations and at different times during a single examination; (3) the apparent ring scotoma itself and its variations (notably the "breaking up" into islets of amblyopia); (4) the difference between the right and the left field of vision; (5) the frequent transitions from ring scotoma to contracted fields; and (6) the spiral contour of the field found occasionally with the tangent screen. Most of these points, in isolation, would indeed seem to suggest a psychogenic disturbance. However, interpreted in conjunction with each other, and with the patient's perceptual difficulties, the same data assume the character of an organic picture.

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27. In many patients of our series with involvement of the occipital lobe, who were followed from the early stages of nearly complete amaurosis through stages of visual disorientation up to the stage of some degree of functional reorganization of the field (Bender, M. B., and Furlow, L. T.: Visual Disturbances Produced by Bilateral Lesions of the Occipital Lobes with Central Scotoma, Arch. Neurol. & Psychiat. **53**:165-170 [March] 1945), improvement was rapid, with regard both to objective signs (field changes) and to subjective complaints. However, it was noted that our patient did improve, particularly with regard to the subjective aspects of his visual defects.

Furthermore, closer analysis of the results will show that the inconsistencies are more apparent than real. Actually, they are due to the variations in the tests themselves (as psychophysiologic situations). The patient's responses varied strictly in accordance with the differences in the stimulus situation.

1. *Discrepancies in the Visual Fields as Plotted on the Tangent Screen and the Perimeter.*—First of all, the continued failure of standard perimetry to reveal ring scotomas or concentric contractions of the fields merely points to the specific role of the tangent screen in visual examinations. For simple physical reasons, only the tangent screen method will bring out a shrinking of the peripheral fields for distant objects (Aubert-Förster phenomenon). The patient's tubular fields obtained under our specified conditions might thus be understood as a variation from the norm, but from one which, in itself, embraces a wide range of varying degrees of concentric contraction.[28] As Goldstein [8b] has pointed out, even a considerable degree of contraction of this sort may be a sign of organic damage.

2. *Fluctuation in Vision.*—A great deal of "fluctuation" is always encountered in testing the peripheral zones of the normal field.[29] This is particularly evident for such performances as the discrimination of patterns. For instance, in testing for the Aubert-Förster phenomenon in the normal subject, the subject complains of the following: "The test lines are visible for a few seconds; they disappear and reappear," or "they appear clearly as two lines for one moment and then merge again into one heavy line." Such fluctuations were manifest in our patient not only in the periphery but in the field as a whole. However, the fluctuation was most pronounced at the periphery and decreased as one approached the center except for the ring zone, in which (originally for the left eye, at least) images became completely obliterated.

3. *Ring Scotoma.*—This ring zone of defective vision in the left eye, as well as the annular region, studded with islets of apparent blindness, in the right eye, were not scotomas in the true sense of the word. It is submitted that ring scotoma as an after-effect of cerebral injury is always a misnomer. For both the distance of the ring zone from the center, as well as its density, its width and even its completeness, varied with different methods of examination. These variations were systematic; i. e., a certain specified method would always decrease, and another method would increase, the apparent field disturbance. Among the factors which increased the amblyopia was primarily the slow continual motion of the target. This (next to prolonged exposure of stationary patterns) led inevitably to obliteration or "extinction" of the image. The obliteration, how-

28. To be sure, the universality of the Aubert-Förster phenomenon in normal observers has more recently been questioned. Freeman [18c] has shown that the inferiority of the periphery in the "large-far constellation" fails to appear when the test objects are kept in one place and only the distance of the test lines from each other is gradually increased. But it appears all the more important that even in Freeman's control experiments the discrimination of distant stationary patterns in the periphery seems to be more difficult than the discrimination of closer patterns of identical retinal size.

29. In the normal visual field, fluctuation in intensity and distinctness, fading of color and similar phenomena are characteristic not only of the periphery but also of the region surrounding the normal blindspot (Foucault, M.: Les sensations visuelles élementaires en dehors de la région centrale de la rétine, Ann. psychol. **22**:1-20, 1920).

ever, was not immediate. The target could be moved centripetally for a brief interval, at the end of which obliteration occurred. Thereby the semblance of a ring scotoma was produced. Moreover, the obliteration was transient; i. e., it actually was only a fluctuation. This explains the appearance of islets of amblyopia or apparent amaurosis. As the slow centripetal motion of the target continued, it invariably became visible again. This was possible because of the physiologic superiority of the central region of the field.

4. *Difference Between Right and Left Field of Vision.*—It will be noted that the apparent ring scotoma in the left eye was more complete than that in the right eye. Furthermore, when, on subsequent examinations, the ring scotoma in the left eye had been replaced by annular zones of islets of impaired vision, the disturbance was again greater than the corresponding, and similar, defects in the right eye. The discrepancy in fields was also observed on perimetric examination: The half-crescent scotoma was found in the periphery of the lower temporal quadrant of the left field of vision; a homonymous scotoma in the right field of vision could not be uncovered. Since the wound of the skull was on the right side, it is presumed that the visual pathways on the right side were injured. This produced the temporal crescent defect in the contralateral eye. In a previous communication,[1b] it was pointed out that objective and subjective visual disturbances were more pronounced in the eye opposite the side of the cerebral lesion. This occurred even in cases in which the plotted scotomas were homonymous and congruent. Inasmuch as our patient had a focal lesion in the right hemisphere, his bilateral visual disturbance (ring scotoma) might have been accentuated in the contralateral (left) field, as found on the tangent screen. In this connection, it will be recalled that the patient's visual after-images fluctuated and contracted more rapidly in tests of the left eye than in those of the right eye, thus corroborating the foregoing observations.

5. *Tubular Fields.*—Centrifugal (outward) motion of targets exposed on the tangent screen led, on the whole, not to the semblance of ring scotoma but to that of a contracted field. Once a certain distance from the point of fixation had been attained, the target became invisible if it was held stationary or moved slowly. This can be understood, again, in terms of a periodic, generalized decrease in excitability of the visual system (fluctuation of the threshold). Rapid motion was appreciated in this peripheral region, so that the contraction of the field (in contrast to the usual hysterical field) was "relative." In other words, the fluctuation indicated that there was a periodic rise in the visual threshold. But this rise was not sufficiently high or continuous to produce a more pronounced and enduring defect in vision, namely, amaurosis in the peripheral field.

6. *The Spiral Field.*—The "spiral field" (like the ring scotoma and the tubular field), which was found on examination on the tangent screen under certain conditions, appeared to be an artefact of the method employed in plotting the field of vision. When the target was introduced along each meridian (in a clockwise or counterclockwise order), the field contracted successively, yielding the picture of a spiral. This was due to cumulative effects of continuous stimulation, which, in turn, led to increasing obliteration in the periphery. The spiral was not obtained with other methods of plotting.

INTERPRETATION

On the surface, it would seem that certain features in our case could be explained in terms of local effects of fatigue. Thus, fluctuation

and obliteration of visual images were increased by three changes in the procedure of testing: (*a*) prolonging the time of exposure, (*b*) increasing the degree of eccentricity of the target and/or the distance of the target from the patient and (*c*) enlarging the area stimulated. Moreover, a spontaneous progressive involvement of the field from the periphery inward, or concentric shrinking, was noted on prolonged exposure of large patterns. This was also found in studies of after-imagery and on examinations with moving stimuli. However, the theory of fatigue is not entirely satisfactory when one considers that recovery of visual function was practically instantaneous on interruption and immediate repetition of any particular test.

We therefore turned to the phenomena of visual extinction for more specific clues: Visual, as well as cutaneous sensory, extinction, we think, is due to a form of rivalry of two or more perceptual processes. This rivalry, which can be demonstrated in the normal person, results in dominance of the stronger, and extinction of the weaker, percept. Such extinction is more apparent in pathologic states, in which the intact or less defective substrate dominates over the more defective substrate.[15] These phenomena were interpreted in the light of the discovery of Dusser de Barenne and McCulloch [29a] that "suppression" in a point in the sensory cortex can be produced by exciting another focus in the same cortical area. In psychologic experiments, Fry [30] found that the image of a flash of light can be "suppressed" by applying another flash of light to adjacent areas of the retina. In orienting our data in terms of extinction, we found that we could explain all the aforementioned features (decrease in function with prolongation of stimulation, etc.) on this basis, rather than on that of fatigue.

Moreover, there are other features in the present case which are in agreement with those previously described in patients who showed extinction in their visual fields [1b]: 1. Tachistoscopic examination failed to bring out any visual defects, while prolonged exposure did. 2. Ring scotoma and tubular fields were found only with slow movement (or prolonged exposure) of targets; rapid movement or brief exposure of targets did not produce such defects in the visual field. 3. Obliteration of images usually started in the periphery of the left lower quadrant, in the region bordering on the absolute (hemicrescent) scotoma, and from there it spread over the whole field. This was

29a. Dusser de Barenne, J. G., and McCulloch, W. S.: Factors for Facilitation and Extinction in the Central Nervous System, J. Neurophysiol. **2**:319-355 (July) 1939.

30. Fry. G. A.: Depression of Activity Aroused by a Flash of Light by Applying a Second Flash Immediately Afterwards to Adjacent Areas of Retina, Am. J. Physiol. **108**:701-707 (June) 1934.

particularly evident for moving stimuli.[31] 4. Double simultaneous stimulation with identical targets to either side of the median line led sometimes to extinction in the left half-field. But this tendency was inconsistent and difficult to interpret because of the continual and irregular fluctuations in different parts of the field.

In the majority of patients observed in our series with visual disturbances, fluctuation and extinction tended to take place in quadrants or half-fields.[32] In the present case the disturbance involved the whole field (although it was most pronounced in the neighborhood of the absolute scotoma). The general involvement of the field produced the semblance of ring scotoma or contracted field with certain methods of plotting. In the act of viewing large patterns, the same general disorder became evident as a gradual "fragmentation" of the patient's field. Even strong configurations, such as concentric circles, were broken up into irregular pieces before they eventually disappeared. This last feature in particular points to the diffuseness of the disturbance in this case. Although a circumscribed lesion in the visual substrate might produce an absolute scotoma surrounded by an area of relative impair-

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31. In this respect, the symptoms shown in this case resemble those observed in 3 other cases in our series. In 1 case, that of a gunshot wound in the right occipitoparietal region near the midline with mild sensory and motor changes in the left lower extremity, no distinct field defects could be demonstrated on the perimeter or the tangent screen. However, with continued exposure of any pattern involving more than the immediate center of the field, the patient complained of a peculiar blacking out, which involved, in succession, three quadrants, leaving intact only one, the right upper homonymous quadrant. The patient then shut his eyes, and his difficulty disappeared immediately, only to reappear after another prolonged (ten to fifteen seconds) exposure. The patient's after-images "decayed" rapidly after first appearing complete; again, this decay took place by way of an almost immediate disappearance of those portions of the after-image which had been exposed to the three involved quadrants. In a similar case, a homonymous defect was noted on the perimeter in the extreme periphery of the right fields, suggesting a late stage in the recovery from an initial right hemianopsia. On the tangent screen, after a few seconds of observation, the whole right half of the field "blacked out," with an illusory inward motion from the periphery to the center. As soon as the patient blinked his eye, the field appeared free again. Such cases of fleeting scotoma, though perhaps related, differ from our present case in that the obliteration occurred in quadrants and half-fields.

32. It is interesting to note that Lashley (Patterns of Cerebral Integration Indicated by Scotomas of Migraine, Arch. Neurol. & Psychiat. **46**:331-339 [Aug.] 1941) postulated slowly progressing "waves" of complete inhibition of visual activity in order to account for the spreading scotomas of migraine.

ment of vision,[33] diffuse lesions produced by head injury (molecular changes in neurons) could implicate the entire visual substrate and field. Such diffuse disturbance would likewise have to account for the occasional difficulties in relative localization in visual space, for the slowing in color perception on the tachistoscope and for the abnormalities of fixation and pursuit. Of particular interest in this connection was the reduction in the threshold for fusion of visual flicker, as well as the patient's difficulty in obtaining good stroboscopic motion; both are consistent with Werner's observations on children with cerebral injury.[34] In experiments with normal subjects, Sanders has shown that prolonged stimulation of a given retinal area "inhibits" stroboscopic motion across this retinal area.[35]

From the foregoing data and interpretations, it is apparent that our patient's visual symptoms were not so bizarre as they first seemed. They showed coherent physiologic patterns and represented a direct, and not a neurotic, response of the organism to the head trauma which had been sustained. This conclusion seems unavoidable despite the fact that we do not know what specific material and physiologic changes in the visual substrate provided the basis for the appearance of increased fluctuation and temporary extinction of images.

In spite of their rarity, these visual disturbances after injury to the brain which (under certain conditions of field taking) manifest themselves as apparent ring scotomas should not be underestimated in their clinical importance. The diffuse, but omnipresent, changes in the visual field can be more incapacitating than more circumscript scotomas, even to the extent of complete hemianopsia. In the present case, the patient's symptoms persisted, with little improvement, for almost a year after his injury.

SUMMARY

After injury to the brain, apparent ring scotomas, concentric contraction of visual fields, shifting and "spiral" fields may be found with

33. Such areas of relative defect may reach far beyond the scotomatous region. Even focal lesions, apparently, can result in a widespread and systematic distortion of the normal cortical patterning of visual processes. Such dynamic alteration in the topologic projection of the peripheral onto the cortical retina has been assumed by us in cases of micropsia, metamorphosis, teleopsia and specific disturbances in the perception of visual space and motion.

34. Werner, H., and Thuma, B. D.: Critical Flicker-Frequency in Children with Brain Injury, Am. J. Psychol. **55**:394-399 (July) 1942; A Deficiency in the Perception of Apparent Motion in Children with Brain Injury, ibid. **55**:58-67 (Jan.) 1942.

35. Sanders, E. H.: Over den invloed van vermoienis op de optische schijnbewegingen (Uit het physiologisch laboratorium der Universiteit van Amsterdam), Nederl. tijdschr. v. geneesk. **65**:1820-1836, 1921.

specific methods of examination of the fields. Different types of fields may be encountered in one and the same case. However, the changes observed vary consistently and directly with the different methods of plotting. This is illustrated in a case which was studied with neurologic, psychophysiologic and phenomenologic methods. The unusual field changes (viz., ring scotomas and contracted and spiral fields), as well as severe disturbances in visual perception (haziness, fragmentation and obliteration of images from the periphery inward), seemed to be produced by a continual fluctuation in the visual threshold for different parts of the field, with concomitant phenomena of extinction. It is concluded that such ring scotomas, despite their variability, have an "organic" basis, as pointed out by Goldstein in 1927.

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CAMPTOCORMIA

To the Editor.—In the discussion on the article entitled "Camptocormia: A Functional Condition of the Back in Neurotic Soldiers," by Lieut. Col. S. A. Sandler, an abstract of which was published in the February 1946 issue of the ARCHIVES, page 158, it is stated (column 2, line 5 of the discussion):

". . . As is generally known, the term camptocormia was coined by Babinski after the last war; he was fond of Greek derivations. In the same volume in which he described camptocormia, he described pithiatism—his term for suggestion neurosis. He is also responsible for the term adiadokokinesis."

It is true that Babinski was fond of Greek derivations and introduced the term adiadokokinesis, but he did not coin the term camptocormia. Without using this special term, A. Souques described this syndrome in soldiers at a meeting of the Société de Neurologie de Paris, Feb. 18, 1915, under the title: "Contractures ou pseudo-contractures hystéro-traumatiques" (*Rev. neurol.* **22**:430, 1914-1915). The term camptocormia appears for the first time in an article by Souques and Rosanoff-Saloff (La campocormie, *Rev. neurol.* **22**:937, 1914-1915). Here, it is said: *"L'un de nous, M. Souques, propose de donner à cette incurvation le nom de camptocormie. . . ."* In an article by Rosanoff-Saloff (Considérations générales sur la camptocormie, *Nouv. iconog. de la Salpêtrière* **28**: 28, 1916-1917) it was stated: *"Le terme de camptocormie donné par M. Souques a ces attitudes est plus exact. . ."* Hysterical kyphosis after trauma had been known long before Souques, as Brodie's disease, from the latter's description in 1879-1880 (Deléarde: De la cyphose hystéro-traumatique [maladie de Brodie] *Gaz. d. hôp.* **75**: 749, 1902).

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News and Comment

THE AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

The following candidates successfully passed the examinations of the American Board of Psychiatry and Neurology, Inc., held at San Francisco, June 25, 1946, and have been certified:

Psychiatry.—Alfred Auerback, San Francisco; Lindsay Eugene Beaton, Tucson, Ariz.; O. L. Bendheim, Phoenix, Ariz.; Major Robert A. Coen, M.C., A.U.S.; Bernard L. Diamond, San Francisco; Floyd Oliver Due, Oakland, Calif.; Malcolm Hedges Finley, San Francisco; Edward Earle Hause, San Francisco; Roy Sears Hubbs, Palo Alto, Calif.; Stephen Elliott Kramer, Pueblo, Colo.; Richard Hooker Lambert, San Mateo, Calif.; David Washington Lester, San Diego, Calif.; Col. Emmett B. Litteral, M.C., U.S.A.; Richard D. Lowenberg, San Francisco; John Morgan Lyon, Denver; John D. Moriarty, Vallejo, Calif.; Herbert Allen Perry, Medical Lake, Wash.; Lieut. Col. Donald B. Peterson, M.C., U.S.A.; David G. Schmidt, Larkspur, Calif.; Capt. Earl J. Simburg, M.C., A.U.S.

Neurology.—Clemson Marsh, Los Angeles; Herman Michael Rosow, Los Angeles.

Psychiatry and Neurology.—Elinor R. Ives, Los Angeles; Henry W. Newman, San Francisco; Charles G. Polan, Seattle; Maier I. Tuchler, San Francisco.

Certification in psychiatry and neurology has been given on record to Isham Kimbell, Fort Custer, Mich.

AMERICAN SOCIETY FOR RESEARCH IN PSYCHOSOMATIC PROBLEMS, INC.

At the third annual meeting of the American Society for Research in Psychosomatic Problems, Inc., held in New York, May 11-12, 1946, the following officers were elected: Adolf Meyer, M.D., honorary president (continued); Edward Weiss, M.D., president, and Edwin G. Zabriskie, M.D., secretary-treasurer (continued).

Council members appointed were: William Dock, M.D.; Flanders Dunbar, M.D. (continued); Roy G. Hoskins, M.D.; Jules Masserman, M.D. (continued); Elizabeth Healy Ross (continued); Leonard G. Rowntree, M.D. (continued); Leon Saul, M.D.; Milton J. E. Senn, M.D. (continued); George Soule, and J. Murray Steele, M.D.

MAJOR HARRY L. FREEMAN AWARDED ARMY COMMENDATION RIBBON

The Transportation Corps Center, Fort Eustis, Va., is proud to announce that Major Harry L. Freedman, Medical Corps, Army of the United States, presently the director of the Mental Hygiene Unit here, and recently awarded the Legion of Merit, has just been awarded the Army Commendation Ribbon by the War Department, United States Army, and by direction of the Secretary of War was authorized to wear that ribbon.

His citation for the Army Commendation Ribbon, received from Major General H. C. Ingles, U. S. A., Chief Signal Officer, United States Army, reads:

"Major Freedman as Director, Mental Hygiene Unit, Headquarters, Eastern Signal Corps Unit Training Center, Fort Monmouth, New Jersey, from 22 December 1941 to 22 November 1943, capably discharged important responsibilities in the organization and operation of a Psychiatric Unit for the reclassification and elimination of maladjusted soldiers."

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

VERTICAL NYSTAGMUS PRODUCED BY PERIPHERAL LABYRINTHINE LESIONS. E. A. SPIEGEL and N. P. SCALA, Arch. Otolaryng. **40**:160 (Sept.) 1944.

Vertical nystagmus is generally considered one of the most important signs in arriving at a differential diagnosis between a lesion of the peripheral labyrinth and a lesion of its central nuclei and pathways. Usually it appears almost exclusively with lesions of the latter type, and it is exceptionally rare with lesions restricted to the vertical canals. Spiegel and Scala observed vertical nystagmus in cats after bilateral puncture of the round window. It was present in 5 of 10 animals; in 1 cat oblique nystagmus appeared, while in the others transitory horizontal undulation of the eyeballs or weak horizontal nystagmus followed the operative procedure. The vertical nystagmus usually was directed toward the upper lid and had a frequency of from 5 to 100 per minute. The vertical nystagmus is thought to be an expression of irritation produced by the escape of perilymph. In later stages following puncture of both round windows, definite symptoms of hypofunction of labyrinthine receptors were found. Similar symptoms may also be noticed after puncture of one of the round windows. Puncture of a round window in cats also induces hypofunction of the maculas, although such an effect may remain unnoticed in otherwise normal animals and may be demonstrated by special methods only. One of these methods is the induction of catalepsy with bulbocapnine.

A different type of vertical nystagmus was observed in further experiments, in which gradually developing paralysis of the labyrinth followed the injection of cocaine hydrochloride into the tympanic cavity. The solution of cocaine diffusing into the inner ear produced signs of labyrinthine paralysis.

The authors believe that the mechanism of these phenomena possibly is that of release of receptors in the semicircular canals from a dampening influence normally originating in the maculas, through partial paralysis of the latter.

RYAN, Philadelphia.

THE RELATIVE POTENCY OF SOME ADRENAL CORTICAL STEROIDS IN THE MUSCLE-WORK TEST. DWIGHT J. INGLE and M. H. KUIZENGA, Endocrinology **36**:218 (March) 1945.

New data are presented to show that the decreased ability of adrenalectomized rats to work is due to adrenal cortex insufficiency and not to operative shock. The study was carried out with the purpose of comparing the effects of various biologically active adrenal cortex steroids on the ability of adrenalectomized rats to work. As the study was carried out, it was found that 17-hydroxycorticosterone was the most active compound; 17-hydroxy-11-dehydroxycorticosterone was second; corticosterone was third, and 11-desoxycorticosterone was much less active than any of the C-11-oxygenated compounds.

PALMER, Philadelphia.

THE METABOLISM OF ACETALDEHYDE WITH ACETOIN FORMATION. E. STOTZ, W. W. WESTERFELD and R. L. BERG, J. Biol. Chem. **152**:41, 1944.

Acetaldehyde is a primary product of alcohol metabolism in the animal body. Together with alcohol, it comprises the equilibrium system activated by the alcohol dehydrogenase system, and its concentration in the blood, particularly in man, rises many fold after administration of alcohol. For this reason it merits

attention, but it is probably of further importance in the general scheme of carbohydrate metabolism. Stotz, Westerfeld and Berg found that acetaldehyde is metabolized when incubated with rat brain homogenates. Its rate of disappearance is greatly accelerated by addition of pyruvate and further increased by addition of diphosphothiamine. Disappearance of pyruvate is also accelerated by the addition of acetaldehyde, but the effect is not so pronounced, owing to an initially high rate of pyruvate metabolism. Acetoin (2-butanone-3-hydroxyacetylmethylcarbinol) is formed nearly quantitatively in rat brain homogenates from acetaldehyde in the presence of pyruvate. The same factors which accelerate disappearance of acetaldehyde also increase formation of acetoin. Brain tissue from thiamine-deficient pigeons shows a notably lower ability to form acetoin from acetaldehyde and pyruvate and is stimulated in this respect to a greater extent than normal pigeon brain by diphosphothiamine. Certain toxic manifestations of acetaldehyde in rats are described, and a procedure was developed whereby formation of acetoin from acetaldehyde was demonstrated in vivo by the appearance of acetoin in the blood.

PAGE, Cleveland.

THE CREATINE AND CREATININE EXCRETION OF NORMAL ADULT MALES. ANTHONY A. ALBANESE and DOROTHY M. WANGERIN, Science **100**:58 (July 21) 1944.

Albanese and Wangerin report their observations on creatine and creatinine excretion in 30 normal adult male subjects studied for thirty-eight to sixty days under normal and experimental dietary conditions. Individual daily variations of 10 to 25 per cent of the total creatinine excreted were observed. However, the creatinine excretion was relatively constant under tremendous variations in the protein intake. The irregularities in creatinine excretion are greater than heretofore assumed, and variations in creatinine output are not necessarily indicative of inaccurate twenty-four hour collection of urine.

A simple modification of the Folin method for determining creatine is described. This technic reveals considerable quantities of creatine that may be present in urine but not detectable with the Folin technic.

The authors' data indicate that creatinuria in the adult male is a normal process, and not a feminine or prepuberal male characteristic.

GUTTMAN, Philadelphia.

Psychiatry and Psychopathology

THE NEUROTIC CONSTITUTION. ELIOT SLATER, J. Neurol. & Psychiat. **6**:1 (Jan.-April) 1943.

Slater made a statistical study of 2,000 neurotic soldiers admitted to one E.M.S. neurosis center. The patients were classified under organic states, head injury, epilepsy, schizophrenia, endogenous depression, mental defect, psychopathic personality, anxiety neurosis, hysteria and reactive depression and into the smaller groups of obsessional neurosis, enuresis and malingering. The various diagnostic groups showed no significant differences with respect to age or religion. The mentally defective patients and patients with endogenous depressions came predominantly from the group of unskilled laborers, and the schizophrenic patients, from sedentary occupations. The frequency of noncommissioned officers was highest in the categories of the obsessive neuroses and the endogenous and reactive depressions. There was a general predominance of the asthenic constitution, while the pyknic habitus was most frequent in the manic-depressive group. An "inhibited" sexual drive was common in all groups, but especially in the mentally defective and psychopathic patients. In 55.7 per cent of the patients there was a positive family history of psychiatric deviation. In 58.8 per cent there was some degree of neurosis in childhood. Almost a quarter of the patients had had previous nervous breakdowns, two thirds of the patients with endogenous depressions having such a history. An abnormal premorbid personality was present in over 40 per

cent of the whole group, especially in schizophrenic patients. The most common abnormal personality traits were undue lability of mood and unsociable and anergic tendencies. A third of the patients were of poor intelligence, and there was a frequent association between subnormal intelligence and hysteria. Preconditioning in the form of a bad environment was especially a factor in the neuroses. Previous service in the Army was high. Among the most common precipitating factors were military stress, separation from family, home worries and physical ill health. These factors were elicited in 50 per cent of patients, especially those with anxiety neuroses. They were insignificant in the other 50 per cent, which was comprised chiefly of patients with schizophrenia, epilepsy, psychopathy, mental deficiency and the organic states. Head injury was significantly high in cases of epilepsy, and various physical handicaps were commonly associated with the neuroses. Anxiety states were usually of more recent origin, while some disorders, such as psychopathic personality, were of long duration. Patients of the latter type might have been kept out of the Army through more adequate screening. The most common and least specific symptoms were depression, anxiety and hypochondriasis, while obsessions were rare and were usually associated with depressive reactions. In patients with neuroses the symptoms were fluid and interchangeable. Nearly 60 per cent of the patients received no specific therapy, treatment being limited by the frequency of low intelligence and constitutional instability and by working conditions. Psychotherapy was used with about one fifth of the patients, and narcosis with about 5 per cent (patients with anxiety neurosis); insulin coma therapy was employed with 18 per cent of schizophrenic patients and with those showing considerable loss of weight. Complete recovery occurred in about 10 per cent, and this number together with the patients showing great improvement comprised 25 per cent of the total series, while three fourths of the patients had to be invalided. Of the number of the latter returned to duty half had a relapse. The highest rates of recovery were obtained among patients with organic states, head injury, anxiety neurosis, hysteria and depression, in that order. The chief prognostic criterion consisted in signs of constitutional instability. A poor prognosis was associated with an asthenic habitus, a positive family history of psychiatric deviation, neurosis in childhood, abnormal personality traits, poor intelligence, unsatisfactory home conditions and a duration of illness exceeding two years. A definite inverse ratio was found between different degrees of constitutional abnormality and resistance to military stress.

The study indicated that the organic state is largely independent of the individual constitution and is mainly dependent on the exogenous factor. In the endogenous states the hereditary disposition was all important. In the neuroses, while the exogenous stress was important, the reaction was principally determined by the constitutional predisposition. The neurotic state, according to the author, is merely an exacerbation of the type of response characteristic of the particular patient. The individual constitution of the neurotic patient determines the form and severity of the symptoms, while the environment controls the time of their manifestation. This neurotic constitution and an inadequate intellectual endowment are the two most important predisposing factors in the nervous breakdown.

MALAMUD, San Francisco.

Diseases of the Spinal Cord

INTERVERTEBRAL DISK INJURY: ANALYSIS FROM AN INDUSTRIAL STANDPOINT. H. C. MARBLE and W. A. BISHOP, J. Indust. Hyg. & Toxicol. **27**:103 (April) 1945.

Marble and Bishop attempt to present impartially some of the facts relating to injury of the intervertebral disk from the standpoint of an industrial surgical clinic. The sources of the material are the records of one of the largest insurance companies in the United States interested in workmen's compensation. The facts

as gathered represent a cross section of the work of both neurosurgeons and orthopedic surgeons throughout the country. Compensable cases represent probably the most important group, since injury to the back in industry is frequent and the results of therapy vital to the future of the patient. Of 496 industrial patients suspected of having sustained herniation of the intervertebral disk, 92, or approximately one fifth, were operated on, while four fifths received other therapy. The 92 cases are analyzed from the standpoint of cost, disability, cause and diagnostic criteria. In less than 50 per cent of cases the result is favorable.

J. A. M. A.

LESIONS OF CERVICAL INTERVERTEBRAL DISK. J. BROWDER and R. WATSON, New York State J. Med. **45**:730 (April 1) 1945.

From a review of the literature, Browder and Watson collected only 69 verified cases of protrusion or herniation of a part of the cervical disk. In this paper they present their experiences with 22 cases in which this lesion had disturbed the function of the cervical portion of the spinal cord and/or nerve roots. In 21 cases the diagnosis was verified at operation and in 1 at necropsy. Three different types of pathologic processes were encountered: (*a*) discrete, oval or rounded nodules projecting into the ventral vertebral canal; (*b*) true dorsal herniations of the nucleus pulposus, and (*c*) ridges of annulus fibrosus surmounting hypertrophic bone at the margins of the adjacent vertebra. A negative reaction to the Queckenstedt test does not exclude the presence of such a lesion. The operative mortality for the series was zero. One patient died before coming to operation.

J. A. M. A.

PRESENT STATUS OF SURGICAL TREATMENT OF SCIATIC AND LUMBOSCIATIC PAIN DUE TO LESIONS OF THE INTERVERTEBRAL DISKS. GERMAN HUGO DICKMANN, Prensa méd. argent. **32**:691 (April 20) 1945.

Twenty-one verified cases of herniated disk are reported from the Rawson Hospital in Buenos Aires. The author advises exploration of the fourth and fifth lumbar intervertebral disks in all cases. If the pain radiates to the anterior aspect of the right thigh, the third lumbar intervertebral disk should also be explored. The laminectomy should be as limited as possible. The lower spine should be stabilized if necessary by fusion. A proper corset should be worn for three or four months after operation. The author does not use myelography routinely unless the total protein of the spinal fluid is 80 mg. per hundred cubic centimeters or over. In only 1 of the 21 cases was such a high protein content noted. Negative myelographic evidence does not exclude the presence of a lesion of the disk. There was actual herniation in one third of the cases; in two thirds the disk was concealed. There were 16 males and 5 females in the series. Sixteen were between 21 and 40 years of age; 1 was 19; 3 were between 41 and 50, and 1 was between 51 and 60. In 12 cases the pain was on the left side; in 8, on the right side, and in 1 it was bilateral. In 16 cases only one disk was involved, and in 3 cases the fourth and fifth lumbar disks, and in 2 cases the third, fourth and fifth lumbar disks were involved. The ankle jerks were absent in 4 cases and diminished in 4 cases; the knee jerks were absent bilaterally in 1 case; the ankle and knee jerks on the same side were not elicited in 1 case; in 2 cases the knee and ankle jerks were not obtained on either side. There were no sensory changes in 15 cases. There was hyperesthesia over the outer aspect of the foot in 4 cases, and in 2 cases hyperesthesia was found on the lateral aspect of the foot and the anterolateral aspect of the leg. There was complete recovery in 10 cases; in 10 cases there was definite improvement. In 1 case sciatic pain recurred seven months after the operation. Section of the fourth lumbar nerve root was done, and the pain disappeared.

SAVITSKY, New York.

Peripheral and Cranial Nerves

MODERN VIEW OF NEURALGIA REFERABLE TO MECKEL'S GANGLION. B. R. DYSART, Arch. Otolaryng. **40**:29 (July) 1944.

Dysart cocainized the sphenopalatine ganglion in 3 cases of corneal ulcer associated with pain. In all instances the pain was relieved, usually within four to five minutes after cocainization. In 2 of the cases there were multiple ulcers, some of which healed. Pain was relieved, but no improvement was noticed in the appearance of the ulcer in the other case. Relief of pain was temporary, and the procedure had to be repeated at various intervals.

The use of the proper technic is important. When a patient is being treated for the first time and his tolerance to cocaine is not known, one must proceed with care. A small amount of 2 per cent cocaine hydrochloride is sprayed into the middle meatus, and a few minutes later the pulse rate is checked. If there is no elevation, 1 drop of 10 per cent cocaine hydrochloride is applied by means of a fine, flexible copper applicator. This is left in place for five minutes. The turbinates should be shrunken thoroughly with a vasoconstrictor drug before an attempt is made to reach the ganglion. One or two puffs of 2 per cent cocaine hydrochloride directed toward the middle turbinate usually produces the desired result. Then, with the tip turned up, the applicator is slid along the lower edge of the middle turbinate without touching it or the septum, if possible. As the posterior wall of the nose is reached, the tip is rotated outward and lifted upward to lie just back of the attachment of the middle turbinate. If no improvement results, a saturated solution of cocaine hydrochloride (90 per cent) is used and is applied for five minutes. At any rise of pulse rate or complaint of the patient's feeling a little faint, the treatment is stopped.

The author believes that cocainization of the sphenopalatine ganglion probably achieves its effects by intercepting nerve impulses, and not by influencing any pathologic process in the ganglion.

RYAN, Philadelphia.

PRESENT STATUS OF DIAGNOSIS AND MANAGEMENT OF MÉNIÈRE'S SYNDROME. HANS BRUNNER, Arch. Otolaryng. **40**:38 (July) 1944.

Ménière's syndrome, according to recent studies, is due to an acute increase of fluid within the internal ear, particularly within the endolymphatic canal of the inferior part of the internal ear. In a typical attack the patient complains of tinnitus, diminished auditory acuity and vertigo. The vertigo is of labyrinthine type. Only vertigo of the type which can be produced by the usual clinical methods of examining the labyrinth should be considered as labyrinthine. Labyrinthine dizziness, which lasts for a certain period and reaches a high degree of intensity, is always accompanied with spontaneous nystagmus. Typical attacks are often followed by what the author calls a Ménière neurosis. This, however, does not present spontaneous nystagmus, and if the latter is found between Ménière attacks it should not be thought of labyrinthine origin but, rather, should be considered indicative of a lesion of the posterior fossa. The evaluation of symptoms becomes difficult when the patient complains only of dizziness or only of tinnitus and deafness. In such instances a definite diagnosis cannot be made until the patient is under observation for a long period.

The cause of Ménière attacks and of Ménière's syndrome may be systemic, cerebral or aural. The syndrome is then called "symptomatic Ménière's syndrome." When no cause can be determined, the condition is designated as "idiopathic Ménière's syndrome." Cases of idiopathic Ménière's syndrome are in the minority, but they have stimulated great interest concerning the cause of the disorder. At present two theories prevail: (1) the metabolic theory and (2) the vascular theory. The metabolic theory is not supported by microscopic study of the human ear, by chemical examination of the blood or by the results of treatment. The vascular theory, propounded by Ménière, is supported by micro-

scopic observations on the human ear, as well as by experiment, and explains the pathologic picture of the idiopathic, as well as the symptomatic, Ménière syndrome. Most frequently the angioneurotic disturbance within the internal ear is due to cerebral arteriosclerosis. Incipient arteriosclerosis of the brain should be considered in every case of Ménière's syndrome in which the first attack takes place between the third and the fifth decade of life and in which there is no evidence of other etiologic factors.

Among the systemic diseases, syphilis, malaria, influenza, the leukemias and virus infections may cause the symptomatic Ménière syndrome. Infrequently, some allergic process may be responsible. A chronic adhesive process of the tympanic cavity is frequently found to produce the symptomatic Ménière syndrome.

Ménière neurosis should always be excluded. When the syndrome is symptomatic, the underlying condition should be treated. There is no satisfactory treatment for the idiopathic Ménière syndrome. If the diagnosis of Ménière syndrome is certain, surgical intervention is indicated only when conservative measures have proved unsuccessful and when the disease is progressive on one side while the other ear is normal.

RYAN, Philadelphia.

PSEUDOMEMBRANOUS ANGINA FOLLOWED BY PARTIAL PHARYNGEAL PARALYSIS. JOSEPH V. M. ROSS, Arch. Otolaryng. **40**:164 (Sept.) 1944.

Ross reports 2 cases of Vincent's (pseudomembranous) angina complicated with late partial pharyngeal paralysis in young German prisoners of war. On admission to the hospital the patients complained of headache, malaise, nausea, sore throat and difficulty in swallowing. The signs were those of Vincent's angina of a severe type, with typical lesions in the throat, dysphagia, fetor oris and submaxillary lymphadenopathy. There was no obvious involvement of the gums. Organisms of Vincent's angina were found in the smears of material taken from the throats. Culture of the same material showed no diphtheria bacilli. With the usual treatment for Vincent's angina, the lesions of the throat disappeared. After being discharged from the hospital, both patients were seen in the clinic within a week. They had had the same complaints: difficulty in phonation, with a nasal twang to the voice, and difficulty in swallowing both solids and fluids, the former causing pain in the throat and the latter causing nasal regurgitation with cough. These symptoms developed fifteen and twenty-three days, respectively, after the original illness. Examination revealed left-sided pharyngeal palsy associated with anesthesia in both cases. With vitamin B complex therapy slow progress was observed.

RYAN, Philadelphia.

A TYPE OF NEURITIS ASSOCIATED WITH MALARIAL FEVER. ABNER M. HARVEY, Bull. Johns Hopkins Hosp. **75**:225 (Oct.) 1944.

Harvey discusses a type of peripheral neuritis which occurs in association with malaria. It is characterized by pain, hyperesthesia and hyperalgesia, increased sweating and a feeling of tightness, with increase in muscle tone accompanied by actual muscular contractions. In cases of the mild form the only abnormalities are transient attacks of numbness and tingling. There is considerable variation in the time of onset of the first neurologic symptoms in relation to the febrile paroxysm.

Of 100 consecutive cases of malaria, symptoms of the milder type alone, without objective neurologic abnormalities, were present in 18 per cent. Harvey observed 16 cases of the more severe type of neuritis.

GUTTMAN, Philadelphia.

REVIEW OF ONE HUNDRED CASES OF DIABETIC NEUROPATHY. A. RUDY and S. H. EPSTEIN, J. Clin. Endocrinol. **5**:92 (Feb.) 1945.

Rudy and Epstein review 100 cases of diabetic neuropathy followed from one to ten years. The incidence according to clinical localization was as follows:

neuritis, 54 cases; myelopathy, 26 cases; encephalopathy, 4 cases; encephalomyelopathy, 5 cases, and neurogenic disturbances of the bladder, 11 cases. Diabetic neuropathy is a generalized neurologic disturbance. It is observed not only in the acute stage of diabetes but also soon after the control of the glycosuria and hyperglycemia and with chronic, and even mild, diabetes. This neuropathy develops most frequently in patients over 50 years of age and is preceded or accompanied by considerable loss of weight. Symptoms and signs of a vitamin B complex deficiency are frequently associated with it. The vitamin deficiency is secondary, and it appears to be caused by the disturbed metabolism and at times by an associated chronic infection or other complication. A demonstrable dietary insufficiency is a factor only in certain cases. Complete recovery from the neuropathy is uncertain and slow, but it occurs after prolonged therapy with vitamin B and control of the glycosuria and hyperglycemia.

J. A. M. A.

Vegetative and Endocrine Systems

EFFECTS OF ADRENOCORTICOTROPIC HORMONE ON THE OSSEOUS SYSTEM IN NORMAL RATS. HERMANN BECKS, MIRIAM E. SIMPSON, CHOH HAO LI and HERBERT M. EVANS, Endocrinology **34**:305 (May) 1944.

The authors have shown that by treating normal rats with a preparation of the adrenocorticotropic hormone both chondrogenesis and osteogenesis are retarded, whereas osteogenesis ceased in hypophysectomized rats. Although lessened food consumption was shown to result in retardation of gain in body weight and bone growth, it did not explain the extent of the retardation in the animals treated with the adrenocorticotropic hormone. In the absence of the adrenal glands, there was shown to be no significant changes in bone or growth inhibition.

PALMER, Philadelphia.

ANTAGONISM OF PITUITARY ADRENOCORTICOTROPIC HORMONE TO THE ACTION OF GROWTH HORMONE ON THE OSSEOUS SYSTEM OF HYPOPHYSECTOMIZED RATS. HERMANN BECKS, MIRIAM E. SIMPSON, WALTER MARX, CHOH HAO LI and HERBERT M. EVANS, Endocrinology **34**:311 (May) 1944.

After hypophysectomy, the proximal epiphysial regions of the tibias of rats were compared when no injections were given and after injections of the adrenocorticotropic hormone of the pituitary, the growth hormone and a combination of the two. The results observed showed that the adrenocorticotropic hormone of the pituitary given alone scarcely affected the inactive condition of the epiphysis; the state of the bone formation was characteristic and similar to that of the controls. The growth hormone activated the cartilage and caused resumption of formation of delicate, straight trabeculae of bone. Simultaneous injection of adrenocorticotropic hormone and growth hormone produced (1) a great decrease in width of the proximal epiphysial cartilage, (2) significant retardation of endochondral bone formation and (3) great decrease in osteoblastic and osteoclastic activity.

PALMER, Philadelphia.

CUSHING'S SYNDROME WITHOUT ADENOMATOUS OR HYPERPLASTIC CHANGES IN PITUITARY BODY OR ADRENAL CORTICES AND COMPLICATED BY ALKALOSIS: REPORT OF CASE WITH NECROPSY. H. E. CLUXTON JR., W. A. BENNETT, M. H. POWER and E. J. KEPLER, J. Clin. Endocrinol. **5**:61 (Feb.) 1945.

Cluxton and his associates report the clinical history and necropsy observations in the case of a woman aged 27 who came to the Mayo Clinic presenting most of the features of Cushing's disease (pituitary basophilism). The absence of adenomas or neoplastic or hyperplastic changes in the pituitary body, thymus or adrenal cortex and the associated alkalosis that was present during the life of the patient are elements of additional interest. The patient's illness could not be

attributed to any demonstrable anatomic abnormality if one expects the hyaline changes that were found in the basophilic cells of the anterior lobe of the pituitary body. The physiologic significance of these changes is not known, but one of the authors believes that these changes are secondary or retrograde rather than an alteration of fundamental significance in the causation of the syndrome and that the clinical manifestations of the patient's illness were an expression of an abnormal function of the adrenal cortex of a hypersecretory character in spite of the fact that there was no histologic evidence to support this view. This case also presents one more instance of alkalosis and low potassium content of the blood occurring with Cushing's syndrome, 3 cases having previously been reported from the Mayo Clinic. In some cases alkalosis occurs solely as the result of abnormal function of the adrenal cortex.

J. A. M. A.

CUSHING'S SYNDROME. EVELYN ANDERSON and WEBB HAYMAKER, J. Nerv. & Ment. Dis. **99**:511 (May) 1944.

Anderson and Haymaker review the controversy as to the pituitary or the adrenocortical origin of Cushing's syndrome. They believe that the demonstration of a substance resembling the hormone of the adrenal cortex in the blood and urine of patients with the disease is evidence of its adrenocortical nature. They report 7 cases of the syndrome. In 4 cases death ensued, and in 3 cases improvement was observed. The occasional cyclic nature of the disease is illustrated in 2 of the cases, in which spontaneous remission occurred. In 2 cases the hair of the scalp changed from blond to black, and in 1 case became coarse. Studies of blood electrolytes revealed that the levels of potassium and sodium in the serum varied from time to time in the same patient, but in some of the cases the serum potassium tended to be at the lower range of normal. This observation may possibly be considered significant as an expression of an excess of adrenocortical hormone. In 2 cases significant amounts of adrenocortical hormone were found in the blood and urine, and in another case the hormone was demonstrated in the urine alone. The adiposity and hypertension which invariably occur with Cushing's syndrome may be due to the effects of the hormone of the adrenal cortex rather than of the androgenic fraction. Albright designated the former as the S hormone and the latter as the N hormone.

CHODOFF, Langley Field, Va.

Treatment, Neurosurgery

SULFADIAZINE AND ITS SODIUM COMPOUND IN TREATMENT OF MENINGOCOCCIC MENINGITIS AND MENINGOCOCCEMIA. EMANUEL APPELBAUM and JACK NELSON, Am. J. M. Sc. **207**:492 (April) 1944.

Appelbaum and Nelson treated 142 patients with meningococcic meningitis by means of sulfadiazine and its sodium compound. One hundred and twenty-six of the 142 patients were treated within the first three days of illness; 115 patients showed definite changes in the mental state, varying from irritability and apathy to delirium and coma. Ninety-two patients had hemorrhagic eruption.

The cerebrospinal fluid showed varying degrees of turbidity, with predominance of polymorphonuclear cells. The sugar was either absent or greatly diminished in almost all patients. The smears of 123 patients showed varying numbers of intracellular and extracellular gram-negative diplococci. In 95 patients the organisms were found both by smear and by culture. The strain of meningococcus was identified in 99 instances of meningitis and in the 8 cases of meningococcemia without meningeal involvement.

On the first day of treatment, children under 1 year of age received from 2 to 3 Gm. of the drug; children from 1 to 3 years of age received from 3 to 4 Gm.; children above that age received from 4 to 7 Gm., and adults, from 9 to 12 Gm. In 89 instances the drug was given intravenously during the first twelve to twenty-four hours, as a rule in a 5 per cent solution in distilled water. Prompt and con-

sistent results were obtained with levels of the drug ranging from 10 to 15 mg. per hundred cubic centimeters in the blood and from 7 to 10 mg. per hundred cubic centimeters in the cerebrospinal fluid.

The patients showed striking clinical improvement on the second or third day of chemotherapy. It was found that chemotherapy might be discontinued after the patient had been afebrile for twenty-four to forty-eight hours and had received a total of 15 to 20 Gm. of the drug. In the fulminating form of the disease, the outstanding clinical feature was the presence of circulatory collapse.

Arthritis occurred in 15 patients. The low incidence of serious complications was remarkable. Toxic reactions due to sulfadiazine were encountered in 42 of the patients. Hematuria was observed in 20 patients. It is necessary to maintain a urinary output of at least 1,200 cc. in each twenty-four hour period.

Drug fever, noted 15 times, was the second most important toxic effect. In 4 cases drug intoxication produced the syndrome of encephalopathy, in which the clinical picture was characterized by varying grades of stupor, often progressing to deep coma. There were only 2 instances of peripheral neuropathy. The presence of initial leukopenia is not a contraindication to the use of chemotherapy.

The authors believe that there is little advantage to be expected from the additional use of the specific serum.

MICHAELS, M.C., A.U.S.

AMPHETAMINE SULFATE IN ABORTING THE ACUTE ALCOHOLIC CYCLE. MICHAEL M. MILLER, Am. J. Psychiat. **100**:800 (May) 1944.

Miller studied the effects of amphetamine sulfate during the period following acute intoxication in 56 nonpsychotic patients with chronic alcoholism. The medical regimen consisted in the administration of 10 mg. of amphetamine sulfate after breakfast and lunch, 0.1 Gm. of phenobarbital on retiring and 30 to 40 mg. of thiamine hydrochloride per day. In 49 patients the drinking cycle was interrupted. In 8 control patients who received placebos the drinking cycle was not disturbed. Single doses of amphetamine sulfate given to semistuporous patients roused them. "Hang-over effects" were greatly reduced. The treatment resulted in improvement of mood, rapport, awareness, sensory perception and activity drive.

FORSTER, Philadelphia.

THROMBOSIS OF THE CAVERNOUS SINUS WITH HEMOLYTIC STREPTOCOCCIC BACTEREMIA. JONAS W. WOLF, Arch. Otolaryng. **40**:33 (July) 1944.

Wolf reports recovery in a case of thrombosis of the cavernous sinus. The patient was a 10 year old boy, and the source of the infection was a furuncle on the bridge of the nose. Associated with the thrombosis were hemolytic streptococcemia and multiple renal and pulmonary thrombi. Over a period of nineteen days the child received 64 Gm. of sulfadiazine and 500,000 Oxford units of penicillin. Therapy was instituted with the administration of sodium sulfadiazine intravenously and of sulfadiazine by mouth. When no change in the patient's condition developed, the sulfadiazine was discontinued and a dose of 60,000 units of penicillin was given intravenously by the continuous drip method. No improvement was noted, and on the fourth day of treatment the patient received 5 Gm. of sodium sulfadiazine and 60,000 units of penicillin intravenously. Use of the two drugs simultaneously brought about complete recovery in the following two weeks.

RYAN, Philadelphia.

NEW ASPECTS OF SPINAL INJURIES. A. G. DAVIS, Arch. Surg. **46**:619 (May) 1943.

In the treatment of spinal fractures and dislocations the following points have been generally accepted: 1. Hyperextension is generally applied for the reduction of fractures. 2. The fractured vertebral body may be depended on to form a callus, as does any other broken bone. 3. In cases of injury to the cord, laminectomy as

a decompressive procedure occupies a place distinctly secondary to that of hyperextension. 4. The Queckenstedt test is an important aid in determination of the presence of subarachnoid block before and after hyperextension. 5. Skeletal traction by means of the Crutchfield clamp is the best method of treatment for crush fractures and fracture dislocations of the cervical region. 6. The intact posterior arches are capable of bearing the weight of the torso without the aid of the vertebral body; hence it is safe for the patient to be ambulatory for part of the period of convalescence. 7. The anterior longitudinal ligament acts as the main reducing medium and as the chief check strap opposed to excessive hyperextension.

There is some disagreement as to the period of convalescence and the method of reduction in cases of compression fracture. The author keeps his patients in the recumbent position for six weeks and then permits them to be ambulatory in a hyperextension cast for another six weeks. In cases of thoracolumbar fractures reduction can best be obtained by the foot suspension method.

Fractures of the laminas, pedicles and articular facets often are not recognizable in roentgenograms. In certain cases of fracture with "locked" dislocation the roentgenographic picture is characteristic. Recognition of these cases is important, because the lesion should not be manipulated but should be treated by open reduction after the dislocation has been "unlocked" in a flexion device.

Since the tensile strength of the anterior longitudinal ligament is great (breaking point, 153 Kg.) and the pull needed for reduction rarely exceeds 36 Kg., there is an ample margin of safety.

A method is described for correction of bilateral cervical dislocation. Certain types of anterior cervical dislocation can easily be corrected in the early stage by a hyperextension collar; if neglected, the dislocation may be progressive and require fusion operation.

LIST, Ann Arbor, Mich.

AMPHETAMINE (BENZEDRINE) SULFATE UPON HIGHER NERVOUS ACTIVITY COMPARED WITH ALCOHOL. NATHANIEL FINKELSTEIN, E. BRYCE ALPERN and W. HORSLEY GANTT, Bull. Johns Hopkins Hosp. **76**:61 (Feb.) 1945.

Finkelstein, Alpern and Gantt studied the effect of amphetamine sulfate and alcohol on a group of 19 subjects. They observed that amphetamine sulfate in oral doses of 10 to 15 and 20 to 30 mg. increased the systolic and diastolic blood pressures of healthy young adults (an average of 13.6 mm. for the systolic and of 10.4 mm. for the diastolic pressure). It did not alter the pulse rate. The resting respiratory rate was increased about 21 per cent. The drug had an effect on motor conditioned reflexes, causing slight improvement in differentiation between positive and negative conditioned stimuli. The threshold of sensation to an electrical shock, the acuity of hearing and the performance with a number series problem test were unchanged by amphetamine.

The presence of a respiratory conditioned reflex under these experimental conditions was observed.

Alcohol had a more pronounced effect on motor conditioned reflexes than amphetamine. Alcohol favored excitatory reactions, interfered with inhibition and tended to convert inhibitory into excitatory reactions, impaired the respiratory conditioned reflexes and greatly increased the threshold for perception and for pain.

The authors conclude that the conditioned reflex test was more sensitive in detecting a change in higher functions of the nervous system than were the verbal tests which were used.

GUTTMAN, Philadelphia.

RESULTS OF MODERN METHODS OF TREATMENT OF POLIOMYELITIS. R. W. JOHNSON JR., J. Bone & Joint Surg. **27**:223 (April) 1945.

Johnson recommends in the acute stage bed rest, sedation for restlessness and pain and half-shell plaster molds or "Toronto" type splints for paralyzed, weakened or tender extremities in positions of relaxation. Frequent checks are made of muscle power. The presence of hyperesthesia or muscle tenderness is also checked.

Except in cases of the encephalitic type, the author has not had clinical evidence of spasticity in the paralyzed extremities. Stiffness of the neck and back is usual in the early days, but this tends to disappear spontaneously. Radiant heat is administered intermittently as a stimulant to local circulation. In the convalescent period gentle massage is administered to the paralyzed or weakened groups and is increased slowly in depth and force as soon as hypersensitivity permits. Limited passive motion is begun in joints when muscle power is below 50 per cent, and active motion is started in an increasing range as the muscles grow in strength. Graduated exercises are given for weakened muscles. Patients who seem destined to have some disability are turned from invalidism and self pity toward an attitude of adaptability and compensation. In the wards the children help one another to achieve this end. Ward patients do much better in this respect than patients in private rooms. Later, underwater exercise in pools is used. The benefit of a crusade of the Sister Kenny type is that it makes physicians reexamine their own therapeutic procedures. Johnson has remained unimpressed by the claims of superiority of the Sister Kenny treatment. Patients are not cured, they recover; and the author does not rate recovery in case units, for misleading statistics are produced in this way. The proper unit is the weakened and paralyzed muscle, and recovery is judged on final muscle power as compared with the original degree of paralysis. The record of each muscle is kept separately. For this analysis the author has selected ten commonly paralyzed and important muscles: the gluteus maximus, gluteus medius, quadriceps, hamstring, gastrocnemius, tibialis anterior, deltoid, biceps humeri, triceps brachii and opponens pollicis muscles. Figures shown in tables concern 64 patients. The paralyzed muscle units reported include 350 in the lower extremity and 106 in the upper extremity. All muscles should have three months of careful and painstaking protection and treatment comparable to that given in cases of peripheral nerve lesions. At the end of such a three month regimen a prognosis of recovery can be arrived at, for the muscles can then be divided into three categories: (*a*) Muscles which have not recovered 30 per cent of power in three months. No return of useful power is to be expected, and these make up the permanently paralyzed extremities. (*b*) Muscles which by this time have 80 per cent or more power and can be counted on to function satisfactorily without further treatment except general supervision. (*c*) The group which has demonstrated some return of power and has a three month level of 30 to 75 per cent. These muscles have potentiality for further recovery to a point where useful function can be restored and are the important ones as far as further active treatment is concerned. No appreciable recovery continues beyond eighteen months even under ideal conditions, but untreated or inadequately treated muscles have been salvaged by this regimen as late as six to ten years after the acute attack, indicating a previous nerve recovery which had been masked or nullified by the overstretching or overfatigue of the muscle or by opposing contracture.

J. A. M. A.

SUBARACHNOID ADMINISTRATION OF PYRIDOXINE HYDROCHLORIDE IN DISEASES OF THE NERVOUS SYSTEM. SIMON STONE, J. Nerv. & Ment. Dis. **100**:185 (Aug.) 1944.

Stone reviews the literature on the uses of pyridoxine in treatment of various diseases of the nervous system and reports its effect in a number of cases when introduced intrathecally. Pyridoxine hydrochloride in 30 to 50 mg. doses mixed with 8 to 10 cc. of spinal fluid was introduced into the lumbar sac of 26 patients, without any untoward results. Intrathecal administration is preferable to other methods because the solution can be placed in greater concentration and in closer contact with the affected nerve roots and involved areas in the spinal cord.

In almost all cases there was improvement in the feeling of well-being of the patients and in their behavior in the ward. Specific improvement was produced in the abnormal movements of Sydenham's chorea, in the rigidity of postencephalitic paralysis agitans, in the weakness and muscular tenderness of peripheral neuritis, in the weakness and contractures of anterior poliomyelitis, in the weak-

ness and paresthesias of infectious meningomyeloradiculitis and in the spasticity and hyperreflexia of multiple sclerosis.

The beneficial results are probably due to the fact that diseased nerve tissue requires greater amounts of thiamine and pyridoxine for proper metabolic function.

CHODOFF, Langley Field, Va.

STUDIES OF FIBRIN FOAM AS A HEMOSTATIC AGENT IN NEUROSURGERY, WITH SPECIAL REFERENCE TO ITS COMPARISON WITH MUSCLE. FRANC D. INGRAM, ORVILLE T. BAILEY and FRANK E. NULSEN, J. Neurosurg. **1**:171 (May) 1944.

A completely satisfactory hemostatic material for neurosurgical work should produce prompt control of bleeding, should give no (or very slight) tissue reaction and should not cause the formation of antibodies. The authors report the results of a number of experiments showing the superiority of fibrin foam and thrombin to other agents.

The escape of a large amount of thrombin into the cerebrospinal fluid is not followed by any serious reactions. As compared with muscle thromboplastin, soaked fibrin foam appeared to have the following advantages: 1. It produces far less tissue reaction. 2. The supply is virtually unlimited. 3. An excess is innocuous. 4. It can be molded to conform to the contour of the bleeding surface. 5. If dislodged free in the ventricle, it can be absorbed. 6. Its use is superior in large bleeding channels, where a large plaque is required. 7. It is usable where muscle could seldom be used, thus saving much time at operation.

There is a considerably greater tissue reaction to black silk and bone wax than to fibrin foam. Furthermore, fibrin foam is better than soluble cellulose in that (1) the foam structure holds the thrombin better than the fibrillar cellulose; (2) the fibrin foam is more readily cut into adaptable shapes and will better retain the contours of the bleeding surface; (3) it is more quickly and permanently adherent to the bleeding surface.

WHITELEY, Philadelphia.

GROSS INTRACEREBRAL HEMATOMAS: REPORT OF 16 SURGICALLY TREATED CASES. W. B. HAMBY, New York State J. Med. **45**:866 (April 15) 1945.

Hamby says that, while the commoner types of intracranial hemorrhage are well known, spontaneous, limited, removable intracerebral hematomas are less familiar. He reports 16 cases of gross intracerebral hematomas that were drained, with recovery in 14 cases and death in 2 cases. Cases of hemorrhage due to cranial injury with skull fracture have not been included in this series. One of the 2 deaths was due to massive pulmonary atelectasis and the other to a fatal recurrent hemorrhage from a ruptured aneurysm of a major cerebral vessel. In 7 cases the hematoma was associated with cerebral arterial disease and in 5 cases with intracerebral neoplasms (metastatic in 3 cases, meningioma in 1 case and astrocytoma in 1 case). In 1 case the hematoma was proved and in 3 cases it was suspected to be due to a ruptured aneurysm of major blood vessels. In 1 case there was delayed post-traumatic intracerebral hemorrhage.

J. A. M. A.

OSTEOMYELITIS OF THE SKULL: ITS TREATMENT WITH PENICILLIN AND REPAIR OF THE DEFECT WITH TANTALUM. M. T. SCHNITKER and W. D. MCCARTNEY, Surgery **18**:94, 1945.

Schnitker and McCartney report 3 cases of acute spreading osteomyelitis of the frontal bone. They believe that penicillin has revolutionized the therapy of osteomyelitis of the skull of sinal origin. It overcomes the infection rapidly, limiting its spread and thus permitting early operation, with primary closure of the wound. The authors use a corneal incision and close the wound primarily without packing, instead of employing the classic inverted T incision and open packing of the wound, thus avoiding a deforming scar of the forehead. The

wound is irrigated with solutions of penicillin through a catheter left in the incision. It is felt that penicillin should be regarded as a bacteriostatic agent. It limits the spread of infection and permits early removal of the infecting nidus. In a few cases recovery occurred after use of penicillin alone, usually in the absence of sequestration.

The infection (nonhemolytic staphylococcus) in the first case reported was well controlled with penicillin but could not be eradicated with this drug. The infection was apparently cured on two occasions but recurred with cessation of treatment with penicillin, which had been administered in doses of 240,000 units daily. A rapid recovery was made after the entire skull anterior to the coronal suture was removed in one piece. A tantalum plate was used to repair the resulting defect in the frontal bone and was inserted seven months after the initial operation.

In the second case osteomyelitis of the frontal bone (aerobic nonhemolytic streptococcus and nonhemolytic Staphylococcus albus) had not responded to sulfonamide therapy and local operations on the sinus. Twelve days after the beginning of penicillin therapy (200,000 units daily) the infection was apparently controlled, and the entire osteomyelitic area was removed through a coronal incision in one piece. The defect was repaired with a tantalum plate, inserted six months later.

In the third case osteomyelitis of the frontal bone was controlled with prolonged penicillin therapy and external, radical excision of the frontal sinus. In this case there was evidence of a mass lesion involving the left frontal lobe. Repeated exploration of this area with the needle gave negative results, and it was concluded that edema of the brain underlying the osteomyelitis was the cause of the symptoms of cerebral abscess.

SHENKIN, Philadelphia.

ADRENALECTOMY IN HYPERTRICHOSIS WITH MENTAL CHANGES. R. GREENE, A. S. PATERSON and G. C. L. PILE, Brit. M. J. **1**:698 (May 19) 1945.

Greene and his associates report the case of a woman aged 25 who had hypertrichosis associated with mental changes, which gradually resolved after adrenalectomy. The psychologic changes preceded the external physical changes. When first seen, she was drifting into a tense hypochondriacal state. The removal of most of the causes of her anxiety did not bring about her recovery. Only after operation was she set on the road to recovery.

J. A. M. A.

INTRAORAL SPLINT FOR FACIAL PALSY. A. G. ALLEN and D. W. C. NORTHFIELD, Lancet **2**:172 (Aug. 5) 1944.

Allen and Northfield describe a new form of splint to prevent stretching of paralyzed facial muscles by antagonists and gravity. This device is an intraoral plastic hook for the corner of the mouth. It is anchored to an artificial plate if the patient is edentulous or against the natural teeth. Each splint is fitted to the individual patient by previously obtaining a plaster impression of the corner of the mouth. The advantages of this splint lie in its lack of irritation, its inconspicuousness and its stability when in place.

MCCARTER, Boston.

Society Transactions

CHICAGO NEUROLOGICAL SOCIETY

Ben W. Lichtenstein, M.D., *President, in the Chair*

Regular Meeting, Oct. 9, 1945

Neurinoma of the Twelfth Nerve. DR. ERNST HAASE.

Neurinoma of the twelfth nerve is a rare tumor. I found reports of only 4 cases, 2 of extracranial and 2 of intracranial tumors. Friedman and Eisenberg (*Ann. Surg.* **101**:834, 1935) and Capella (*Rev di chir.* **2**:169, 1936) successfully removed neurinomas of the hypoglossal nerve in its extracranial course. Capella's case was one of generalized familial neurofibromatosis. De Martel (1933) operated on a tumor in the intracranial course of the hypoglossal nerve, the growth being attached to the canalis hypoglossi. Bailey, Buchanan and Bucy reported the case of a typical neurinoma of the right hypoglossal nerve deeply indenting the bulb; in addition, there were neurofibromatous involvement of many peripheral and sympathetic nerves and of the extracranial portions of the ninth to the twelfth nerve, spongioblastoma of the optic chiasm, astrocytoma of the cerebellum and gliomatous nodules in the cerebral and cerebellar cortex.

In my first case the tumor was not correctly diagnosed because the clinical picture was confusing, showing, in addition to atrophy of the left half of the tongue with fibrillation, Argyll Robertson pupils and involvement of the left trigeminal, facial and acoustic nerves and the right accessory nerve, as well as spastic paresis and sensory disturbance of the right side of the body and diminished appreciation of pain and temperature on the left side between the second cervical and the eleventh thoracic nerve. Necropsy showed a neurinoma of the left hypoglossal nerve almost completely filling the foramen magnum invading the occipital bone and extending laterally to the internal acoustic meatus. Unfortunately, the spinal cord was not examined.

In the second case, in which the correct diagnosis was made and operation performed by Dr. Bucy, a roentgenogram of the base of the skull revealed erosion of the occipital bone around the left canalis hypoglossi. The patient had complained of a tickling sensation in the throat, coughing and choking on swallowing, dizziness and pains in the left suboccipital region. The left half of the tongue was atrophic and fibrillating; the left glossopharyngeal and accessory nerves were slightly involved. Two tumors of the intracranial portion of the left hypoglossal nerve were removed and found to be neurinomas.

DISCUSSION

DR GEORGE B. HASSIN: Some features of Dr. Haase's cases pertain to involvement of the ninth, tenth, eleventh and twelfth cranial nerves, especially in the second case; in the first case the involvement was less extensive. Combined extracranial involvement of the aforementioned nerves, of all or of several of them only, always indicates, in my opinion, a surgical condition in the form of a foreign body or a tumor. Such a lesion may be suspected and located even before roentgenographic examination has been made. I know of a case in which the last four cranial nerves were affected by a calcified lymph node of the neck at the jugular foramen. Nothing could be palpated or visualized, and only the history and the clinical picture of the syndrome of the jugular foramen, that is, involvement of the ninth, tenth, eleventh and twelfth nerves, suggested pressure by a lymph node. This diagnosis was borne out by roentgenographic examination

and subsequent operation. A number of contributions have appeared in which the cause of the syndrome of the jugular foramen was a bullet, but few in which the cause was a tumor, as recorded by Dr. Haase. The lesion may not be demonstrable, but, as has been stated, it may be suspected on the basis of the combined involvement of some of the four last cranial nerves.

There are certain features in the first case of Dr. Haase which I cannot understand. The Argyll Robertson pupil and other signs of involvement of the central nervous system certainly had nothing to do with the implication of the cranial nerves unless there was pressure on the medulla. Dr. Haase may be able to explain them.

DR. ERNST HAASE: I do not think I can explain these symptoms. Had the spinal cord been examined, an explanation might have been found.

Cerebral Thromboangiitis Obliterans. DR. GEORGE PERRET.

Of a series of 9 verified cases of cerebral thromboangiitis obliterans, 1 in which the diagnosis had been made clinically was presented and discussed. A woman aged 42, of Irish descent, had had transient headaches, attacks of diplopia and difficulty in reading for four years, the symptoms following a slight infection of the upper respiratory tract. Later she had bilateral defects of the visual fields, more severe attacks of diplopia, transient paresthesias on the left side and an episode of aphasia; still later, she had repeated attacks of paresthesias and progressive speech and reading difficulties. When hospitalized in March 1945, she had right homonymous hemianopsia; hesitancy of speech; complete alexia, being able only to spell out words; increased deep reflexes on the right side, and changes of personality. Except for a mottled appearance of the extremities she had no other peripheral vascular disturbances. Roentgenographic studies of the skull, spinal puncture and electroencephalographic examination revealed no abnormalities; the blood pressure was 150 mm. of mercury systolic and 90 mm. diastolic. Ventriculographic studies showed dilated ventricles and enlarged subarachnoid spaces, and a diagnosis of cerebral thromboangiitis obliterans was made. This was verified at operation. An osteoplastic craniotomy on the left side exposed a thickened and opaque arachnoid with large subarachnoid spaces and numerous small, white, stringlike vessels, which were completely obliterated, distributed over the frontal and parietal lobes. The underlying gyri were yellow and atrophied. An obliterated artery was removed for microscopic study.

The vessels were completely occluded with proliferated endothelial and subendothelial connective tissue, and only a few small recanalized channels were present. There was no sign of fresh inflammatory reaction, and the internal elastic membrane was intact. The lesion was confined to the inner layer of the vessel. The surrounding arachnoid was fibrotic as a result of earlier perivascular infiltration. The obliterated vessels were small arteries, scattered over the entire cortex. They were much smaller and more elastic than arteriosclerotic vessels and failed to show the characteristics of periarteritis nodosa. The disturbance of blood supply to the various cortical areas affected resulted in cortical necrosis and atrophy. The transient symptoms favor the hypothesis that angiospasm is the etiologic factor in producing the changes in the endothelial cells. No known therapy has been reported for this type of thromboangiitis obliterans. Spatz, Lindenberg, Foerster, Scheinker and others have reported similar cases in which the condition was recognized at autopsy.

DISCUSSION

DR. L. J. POLLOCK: It is useful to present cases of a type which afford so much difficulty in diagnosis. I am grateful to Dr. Perret for reporting the existence of cerebral thromboangiitis.

DR. VICTOR E. GONDA: I wonder whether an arteriographic examination would help in the diagnosis, I should like to ask whether this was tried and, if so, whether it was successful.

DR. RICHARD B. RICHTER: I wish to ask Dr. Perret whether he believes that the vascular lesions in cases of cerebral thromboangiitis obliterans are similar etiologically to those of the peripheral type and whether he thinks that the vascular lesions, in some cases at least, may not be the consequence of an infectious or a toxi-infectious process. It is perhaps significant that the symptoms in Dr. Perret's first case began after an infection of the upper respiratory tract. The infectious or toxic origin of this type of vasculitis might well be diverse, rather than specific. For example, several years ago I described the case of a boy 14 who died four months after a typical attack of poliomyelitis, which occurred during an epidemic of the disease. Pathologically, in addition to inflammatory reactions and neuronal destruction in the spinal cord and brain stem, which were consistent with a diagnosis of poliomyelitis, there were widespread productive changes in the walls of the smaller arteries of the brain and cord. These were chiefly in the intima of the vessels and were sufficiently great to occlude some of them and so lead to foci of softening.

DR. R. P. MACKAY: What percentage of the 9 patients reported were women? It is known that peripheral thromboangiitis is rare among women.

DR. BEN W. LICHTENSTEIN: I enjoyed Dr. Perret's presentation, but I wish to point out that verification of the diagnosis of cerebral thromboangiitis obliterans is a problem for the histopathologist. The microscopic sections shown on the screen do not reveal any evidence of angiitis, that is, inflammation within the component portions of the blood vessel. The lesion presented may have been healed, but the fact that the tunica elastica appears intact makes it improbable that any severe inflammation was present at any time. The thrombosis may have been the result of any one of many other disorders.

DR. GEORGE PERRET: In answer to Dr. Gonda, Sorgo has published reports of cases in which cerebral arteriographic examination gave evidence of obstruction of vessels.

In reply to Dr. Richter: In some of the cases symptoms followed a history of infection; in others they did not. One woman gave a history of falling while skiing, and shortly thereafter paresthesias developed, which were not related to the site of her injury. It is possible that infectious processes may be an etiologic factor in thromboangiitis obliterans. Spatz also reported cases in which vascular symptoms developed after infectious diseases, but at no time could he prove the presence of organisms or of other manifestations of infection in the vessels or the perivascular tissues. He expressed the belief that cerebral thromboangiitis obliterans was a primary process which occurred in the cerebral vessels and produced the same changes as those in the peripheral vessels of the extremities.

In the present series, 4 of the patients were women and 5 were men. My colleagues and I have also seen cases of peripheral thromboangiitis obliterans in women. We have been able to help patients with this condition by performing lumbar sympathectomies. This operation is helpful in the peripheral type of this disease. I do not know whether cervical sympathectomy, as suggested by Foerster, would help the cerebral type.

The slides were studied by competent pathologists, and all agreed as to the presence of proliferated endothelial and subendothelial connective tissue which completely obliterated the lumen of the vessels, as is characteristic of thromboangiitis obliterans. I refer Dr. Lichtenstein to the beautiful photomicrographs published by Spatz and Lindenberg, which are similar to those I showed tonight. I am sorry I do not have any slides illustrating the early pathologic changes in the vessels; it was found better for the patient to remove for study only completely obliterated vessels.

Contractures Following Experimentally Produced Lesions of the Peripheral Nerves. DR. IRVING C. SHERMAN.

This report deals with the development and treatment of contractures in the muscles of the cat's leg following experimentally produced lesions of the sciatic

nerve without the complication of any contiguous injury. In general, three types of lesions of the sciatic nerve were available: (*a*) denervation; (*b*) primary suture, and (*c*) delayed suture, i. e., secondary operation performed sixty days after the original section, with suture of the nerve. The following therapeutic regimens were carried out: (*a*) no treatment; (*b*) massage and passive motion for five minutes daily; (*c*) massage, passive motion and electrotherapy for five minutes daily, and (*d*) massage, passive motion and electrotherapy for fifteen minutes daily. All treatment was given under the constant supervision of an approved physical therapeutist.

Contractures developed in the denervated muscles in 100 per cent of cases if they were maintained in a shortened position for from forty-five to one hundred and five days. Treatment did not influence this. After section of the sciatic nerve and suture, without immobilization, contractures developed frequently in one or more muscles below the knee. Ninety days after primary suture the incidence of contractures was 84.2 per cent; after delayed suture it was 100 per cent. Contractures were most frequent in the dorsiflexors of the foot because of the spontaneous maintenance of a shortened position when the animal rested. Contracture in one group of muscles tended to prevent it in opposing muscles.

In untreated animals contractures of the dorsiflexors of the foot were less frequent, less severe and less persistent after primary suture than after secondary suture; with the former the peak frequency was 47.1 per cent after ninety days, and with the latter, 72.7 per cent after forty-five days. Massage and passive motion definitely decreased the frequency and severity of contractures after primary suture, the peak frequency being 21.7 per cent after sixty days. After delayed suture, similar treatment seemed to delay development of the peak frequency at forty-five days and undoubtedly decreased the severity of the contractures.

Addition of electrotherapy to massage and, passive motion delayed the appearance of contractures in animals with primary sutures; however, after sixty days it seemed to nullify the influence of massage and passive motion. The longer the period of electrotherapy, the more closely the frequency and severity of contractures approximated those for untreated animals; in general, electrotherapy for animals with delayed suture had no beneficial influence. Furthermore, it favored development of contractures in the unparalyzed antagonists of paralyzed muscles.

Spontaneous movement after recovery of function was as good as, or better than, any form of artificial treatment. After delayed suture residual contractures were similar in frequency and severity in treated and in untreated animals. Contractures were more frequent if the extremity was immobilized than if it was permitted to be free.

DISCUSSION

DR. VICTOR E. GONDA: Would Dr. Sherman tell us what type of electrical treatment was used? Had the status of degeneration been determined by testing with electricity for reaction of degeneration?

DR. PERCIVAL BAILEY: Does Dr. Sherman have any explanation of the increased contracture after electric therapy?

DR. L. J. POLLOCK: May I presume to answer the last question, which is concerned with electrodiagnosis? Dr. Sherman's report is part of a study which my colleagues and I have made on experimentally produced lesions of peripheral nerves in cats. This investigation included studies of motion, sensation, atrophy and fibrillation, as well as the orthodox methods of electrodiagnosis. From this there has developed an accurate method of study in kinetics of stimulation of muscles. It follows, therefore, that we have ample data on reaction of degeneration. There is no correlation between contracture and the kinetics of stimulation. We do not have any data which would explain the incidence of a greater number of contractures in electrically treated animals. We have observed that spontaneous fibrillation continues for a longer period in animals so treated.

DR. GEORGE PERRET: I should like to ask whether there is any relation between the contracted muscles and the ankylosis of the joints.

DR. IRVING C. SHERMAN: In reply to Dr. Perret's question: Each animal was carefully examined after death. The tendons about the joint were divided, and if complete mobility of the joint could not be obtained the animal was discarded. Furthermore, the joints were examined for gross pathologic changes.

I cannot answer Dr. Bailey's question as to the effect of electrotherapy on the frequency and severity of contracture. It may be clarified by histologic studies.

Dr. Gonda asked what type of electrical treatment was employed. A 60 cycle alternating current was used. A mechanical appliance was set up so that the stimuli were delivered at regular intervals, in order to produce a good contraction of the muscle. In the group treated for five minutes daily 12 stimuli were given per minute; in the animals treated for fifteen minutes 40 submaximal tetanic contractions were produced each minute, to conform to the type of treatment given by Guttmann and his group.

The Brain After Intermittent Exposure to Simulated High Altitude.
DR. ARTHUR V. JENSEN and DR. WILLIAM F. WINDLE.

The present study was undertaken to determine possible effects on nerve cells of exposure to tolerably low partial pressures of oxygen intermittently over relatively long periods. Young adult male guinea pigs were subjected to a simulated altitude of 23,000 feet (7,600 meters) six hours a day for six days a week until they had accumulated totals of one hundred, two hundred, three hundred and five hundred hours in a decompression chamber. At appropriate periods experimental animals and controls were killed. This was done, with the animal under pentobarbital anesthesia, by perfusion through the vascular system of a dilute concentration of solution of formaldehyde U. S. P., in order to obtain fixation of the nervous system and other organs in situ. The brain was removed and placed in fixing fluid for several days. It was sectioned serially and every tenth section was stained with an improved buffered thionine technic at a p_H of approximately 4.5. In some experiments the Weil method for myelin sheaths was employed.

Animals gained weight throughout the period of the experiment and exhibited no symptoms of cerebral damage. Acclimatization took place, the number of red corpuscles and the hemoglobin value of the blood increasing significantly after two hundred hours.

Careful comparison of sections through the brains of experimental animals and of the controls revealed no hemorrhages, vascular changes or glial proliferation. No cytologic alterations in nerve cells could be seen. No reduction in the number of nerve cells could be detected by inspection. No changes in the myelin sheaths of nerve fibers and no abnormalities in the fiber tracts of the brain were observed.

Further experiments are in progress to study possible effects of exposure to even lower partial pressures of oxygen, and one of these has been completed. Guinea pigs intermittently subjected to an altitude pressure simulating 23,000 feet for one hundred hours and then to an altitude of 30,000 feet (10,000 meters) for another one hundred hours showed no overt symptoms of injury to the brain, although 1 animal exhibited transient vestibular signs. Four of the animals were studied histologically. Each had focal areas of necrosis in the cerebellum. No generalized cytopathologic change was exhibited.

DISCUSSION

DR. WILLIAM F. WINDLE: We fully expected to see pathologic changes in animals exposed to an altitude of 23,000 feet. Dr. Becker and I had studied the effect of asphyxia in the newborn and had clearly demonstrated not only marked cytopathologic changes, but also gross lesions, correlated with changes in behavior and in learning ability. That was the background with which Dr. Jensen and I entered this study. We have not put our altitude animals to psychologic tests, although we plan to do so. We observed no overt changes in behavior even after exposure to an altitude of 30,000 feet, with the sole exception of the animal that rolled onto its side. The animals were apparently normal. Histopathologic

changes, we are convinced, are not present. We could find nothing with the fairly well controlled methods. We do not hold that there are not some, perhaps chemical, changes.

I do not doubt there is some impairment while the animals are at altitude, but when they are down one cannot see anything. Of course this study concerned guinea pigs. We are aware of the observations of the air corps; they are dealing with men. We were surprised not to observe hemorrhages and other changes, but we are reporting what we found at 23,000 feet—that is—nothing.

Ben Lichtenstein, M.D., *President, in the Chair*

Regular Meeting, Nov. 13, 1945

Cerebral Schistosomiasis: Report of a Case. Dr. I. Joshua Speigel.

Acute Myelitis: Clinicopathologic Study of a Case. Dr. George B. Hassin and Dr. Samuel B. Broder.

A frequent cause of acute paraplegia may be acute myelitis, as is evident in the case reported here. A white man, aged 46, complained of weakness in the legs following an acute infection of the upper respiratory tract. Since the neurologic examination revealed no abnormality, his condition was thought to be functional; and after hypnosis and galvanic stimulation he was able to return to work. Six weeks later there suddenly developed paraplegia and urinary and fecal incontinence, as well as a sharp sensory level for all modalities at the eighth dorsal dermatome and hyperthermia (105 F.). Repeated spinal punctures revealed leukocyte counts varying from 10,700 to 28,000 cells, a positive Pandy reaction and normal dynamics. Since penicillin and sulfonamide drugs failed to lower his temperature permanently and since an epidural abscess was suspected, a laminectomy was performed, with negative results. The patient died on the forty-second postoperative day.

Histopathologic observations revealed dense infiltrations of some blood vessels in the gray and especially in the white substance of the spinal cord with lymphocytes and plasma cells, and of other vessels with compound fat granule corpuscles; there were scattered areas of softening and necrosis, with vast disruption of the white substance in areas which were especially involved, such as the thoracic. The nerve cells of the gray matter remained unaffected, while the meninges were for the most part infiltrated with lymphocytes. The subarachnoid space and some spinal roots, especially at the level of the softened segments of the spinal cord, were packed with compound fat granule bodies. The changes were comparatively mild in the cervical and sacral segments of the spinal cord, and in the medulla, brain stem and cortex they were mostly proliferative (productive), in the form of newly formed capillaries.

Of the changes described, the inflammatory ones (myelitis) were primary, and on them were superimposed those of softening and necrosis, which were either the sequels of toxemia or the manifestation of an anaphylactic reaction of the spinal cord to an infection (evidently respiratory).

Return of Sensation After Denervation and Regeneration of Sutured Nerves. Dr. Eli L. Tigay, Dr. Maurice A. Schiller and Dr. Irving C. Sherman.

Immediately after severance of the nerve there is a loss of touch sense and, to a less degree, of temperature sense over the area of anatomic sensory supply. Within this area is a narrow intermediate zone, adjacent to the border in which pinprick and extremes of temperature are felt. The remaining central zone is completely insensitive. Head and his group expressed the belief that this pattern

of sensory change is due to morphologically different systems in the afferent pathway—one serving epicritic and the other protopathic sensation. Preservation of pain sensation in the intermediate zone of about 1 cm. width is due to dual innervation from adjacent nerves, as shown by Woolard, Waddell and Harpman. For a period after nerve section, the recovery of pain sense within certain areas of the anatomic supply may occur as a result of overlap, as described by Pollock. He found that this sensation returned by shrinkage of the analgesic area as time progressed. Later, Weddell, Gutmann and Guttmann demonstrated that this shrinkage is due to the ingrowth of nerve fibers from surrounding normal nerves. Thus it is seen that the early return of pain sense within the anatomic border of the severed nerve is not due, as proposed by Head, to an accelerated regeneration of protopathic fibers but is the result of an ingrowth of uninjured adjacent nerves.

That area of skin which remains analgesic, however long the period which has elapsed after denervation, was designated the isolated supply of the nerve. Sensation returning within this area could occur only as a result of regeneration of the injured nerve.

In denervations of the sciatic nerve in cats the recovery of pain sensation as a result of overlap can be demonstrated. This occurs within the borders of the anatomic sensory supply when no regeneration is possible. As in man, so in the cat—recovery of sensation resulting from regeneration is often characterized by relatively large areas of skin becoming imperfectly sensitive, in contrast to the shrinkage of areas of analgesia resulting from nerve overlap.

A suture delayed for sixty days after section results in delay in beginning of recovery of sensation, incompleteness of recovery or, in some cases, failure of recovery.

One Component of the Extrapyramidal System. Dr. W. S. McCulloch, Dr. Ruth Rhines and Dr. H. W. Magoun.

By strychninizing the cortex and recording the electrical activity of the brain stem of the monkey, a pathway has been found to arise from area 4-S and diverge from the corticospinal tract in the pons to reach the bulbar reticular formation. Electrical stimulation of the bulbar reticular formation in the cat and monkey has been found to exert a general inhibitory influence on motor activity, whether induced reflexly from the brain stem in an animal with decerebrate rigidity or from the motor cortex. This influence appears to be mediated by reticulospinal connections descending in the anterior portion of the spinal cord. As is evident from its physiologic properties, this corticobulboreticular and reticulospinal pathway is an extrapyramidal system mediating relaxation.

DISCUSSION

Dr. Percival Bailey: I wonder whether the society realizes the importance of this contribution. It is the first time an extrapyramidal system has been pinned down, classified and defined.

PHILADELPHIA PSYCHIATRIC SOCIETY

O. Spurgeon English, M.D., *Presiding*

Regular Meeting, Oct. 12, 1945

Evaluation of Results of Electric Shock Treatment of the Psychoneuroses. Dr. Martin H. Robinson.

This study was carried out in an attempt to determine whether electroconvulsive therapy has any place in the treatment of the psychoneuroses. Sixty-six cases were included: 19 cases of reactive depression, 34 cases of anxiety state, 5 cases of conversion hysteria, 6 cases of obsessive-compulsive neurosis and 2 cases of hypochondriasis. Remissions occurred in 21 per cent of all cases. This number included cases of reactive depressions and anxiety states. Improvement was

observed in 54 per cent of the total number of cases. The precipitating factors included marital discord, sexual problems and disruption of the home.

Conversion hysterias and hypochondriases were least benefited.

Obsessive-compulsive states showed some significant improvement, and it is felt that a longer series of electric shock treatments is required in cases of this disturbance. The most frequent symptoms noted in the series were depression, anxiety, somatic pains, insomnia and lack of interest. Electroconvulsive therapy was most helpful in removing affective distress. It also made the patient more accessible to psychotherapeutic efforts.

The treatment of psychoneuroses has no specific measures or any short cuts. The symptoms are often incapacitating and long drawn out. Electroconvulsive therapy is worthy of consideration in that it removes many of the affective disabilities, shortens the period of disablement and makes the patient more amenable and accessible to psychotherapeutic efforts.

DISCUSSION

DR. J. C. YASKIN: This is an important paper, considering that most extramural psychiatric patients are psychoneurotic. Any aid one can obtain in shortening the period of psychotherapy is very useful. Dr. Robinson's presentation is factual. At least, his results correspond with those obtained in patients who have come under my own observation. A few comments may be pertinent. I believe that electric shock therapy will relieve depression, certain types of anxiety and certain tension situations and that there will be an improvement in the sleep cycle. I do not believe that electric shock therapy will influence one iota the fundamental disorder of the psychoneurosis, the compulsive-obsessive neurosis or the anxiety hysterias, which constitute 65 per cent of all psychoneuroses. I believe that in the treatment of patients who have become extremely depressed and suicidal one has the choice of prolonged narcosis, prolonged hospitalization and shock therapy. Dr. Robinson has already said that electric shock therapy does not take the place of psychotherapy with these patients.

I am not altogether in agreement with Dr. Robinson regarding the large percentage of patients with reactive depressions. It is hard for me to conceive that 19 of some 60 patients had reactive depressions. In my experience, most psychoneurotic patients have proved rather to have manic-depressive psychosis, and they have been amenable to electroconvulsive treatment. Some have proved to be schizophrenic. I do not believe that many patients with an obsessive-compulsive state are benefited, but I should like to caution that many patients with so-called obsessive-compulsive psychoneurosis have actually a manic-depressive psychosis, depressed type, with compulsive trends. If a person has no symptoms up to the age of 35 and there then develops a depression with compulsive trends, this is not an obsessive-compulsive neurosis. Such patients will receive considerable benefit from shock therapy.

Lastly, I should like to emphasize that electric shock therapy should not be used with psychoneurotic patients amenable to other forms of psychotherapy. If the patient can keep her job or do her housework, it is better to resort to psychotherapy than to take a short cut, which is not a permanent cure.

DR. HERBERT FREED: I agree with Dr. Yaskin that this procedure should be an aid to treatment and not the essence of therapy. If the patient can work or make a social adjustment, he should not be institutionalized. Patients cannot be given psychotherapy while they are in the midst of a depression or while caught in the throes of anxiety.

It has been my experience that in certain cases shock therapy will remove a sufficient quantity of depression or anxiety to make a therapeutic interview feasible. Kalinowsky claimed that he did not obtain good results in patients with anxiety neuroses. Dr. Robinson reports that the results were satisfactory in a fairly high percentage of patients. I, too, have had some good results in a smaller series.

I should emphasize again that the foundation for permanent results in treatment of these entities lies in giving the patient insight into the basis of his anxiety, such as repressed hostility or aggression, an insight which can come only with psychotherapy.

DR. CHARLES I. OLLER: The impression I have gained from my rather limited experience with psychoneurotic patients treated with electric shock is that they have not been much benefited by it. The usual story, particularly with psychasthenic persons, is that after a little they are right back where they started. I wonder whether the mere fact that the psychoneurotic patient is hospitalized for four or five weeks—that he is away from home, family and usual responsibilities, does not of itself contribute to the improvement that is seen. Along the same lines, I wonder whether electric shock therapy applied on an ambulatory basis to such patients would not give similarly favorable results.

DR. S. DEWITT LUDLUM: I hesitate to say what I think about it. It would take too long. It seems to me that the reality could be better understood in the light of experiments reported by Gellhorn. He thinks that shock treatment works on the autonomic nervous system. He trained rats to conditioned reflexes. When he gave them electric shock treatments, they lost their newly conditioned reflexes and reverted to their normal reflexes. In the case of the patient with a mental disease, his symptoms represent a new conditioning. If something can be done to blot this out, he will revert to his original conditioning. A change is produced in the blood proteins, in the blood pressure and the temperature and in the mental symptoms. It occurs in rats, and it occurs in people. There is a physiologic basis, and when through electric shock therapy the patient is made to revert to his original conditioning he has normal thinking. These physiologic symptoms of conditioning provide a method of measuring the number of shocks necessary to return the patient to his normal physiologic state.

DR. LESLIE R. ANGUS, Hartford, Conn.: Two questions come to mind. The first concerns the way in which the psychotherapy was used: Was an attempt made to give it in the immediate postshock state, when the patient was more receptive to therapy; or was it carried out consistently over the period between the shock treatments?

The second question is a practical one, based on the fact that some of the patients coming for psychiatric treatment have read articles in the newspapers and magazines and demand shock therapy. In cases in which there is doubt as to the advisability of the treatment, one of the factors in arriving at a decision is whether the treatment, if used, would do harm. In the present series, were there any adverse effects from carrying out the shock therapy over a long period? Dr. Robinson did not mention any, even when patients had received over twenty treatments. Did any spontaneous convulsions follow the shock treatment?

LIEUT. ROBERT KIMMICK, M.C., A.U.S.: I have little to add except that the situation is somewhat different at the Army general hospital with which I am associated. We have selected pretty carefully only psychotic patients. A few psychoneurotic patients have come under treatment, with only fairly satisfactory results. It is mainly the depression and agitation of the patients that seem relieved. The more basic patterns remain. The few patients treated with only partial improvement had reactive depressions. The reactive depressions, as a rule, have cleared up rather quickly without shock therapy because of the causative factors in the Army setup.

DR. MARTIN H. ROBINSON: I want to thank all the discussants for their interesting and valuable comments. I agree that this treatment is most effective in patients showing pronounced affective disorders. I believe that electric shock treatment will lift them out of that state and put them in a frame of mind in which psychotherapy can do something for them. Dr. Yaskin raised the question whether the percentage of cases of reactive depressions was not rather high. At times it is difficult to differentiate between reactive depression and manic-

depressive psychosis, depressed type. I am beginning to feel that it does not matter which of the two labels is applied.

With respect to the obsessive-compulsive neuroses, the series presented was rather short, but from my experience there does not seem to be any very effective treatment for this disorder. Psychoanalysis, perhaps, would offer some hope. Psychoanalysts themselves are cautious in their predictions. Another measure being used is prefrontal lobotomy, but I think electric shock should be tried before anything so drastic as that is carried out.

Dr. Freed, in a sense, agrees that the treatment is valuable in the acute emergency, when the patient becomes a problem at home; if electric shock therapy can abort the attack and make the patient more accessible to psychotherapy, it is worth a trial.

Dr. Oller raised an interesting point as to whether hospital care in itself might be just as beneficial as shock therapy. I did not carry out any control study on this point. Therefore I cannot give any definite answer.

Dr. Ludlum's observations are valuable. They bring up the old controversy: Is the psychoneurosis on a functional or an organic basis? I believe I mentioned the theory of Moriarty and Weil that electric shock has an organic effect on the hypothalamus.

With regard to Dr. Angus' question as to when psychotherapy is effective: The purpose is to gain rapport with the patient and attempt some transference. Obviously, it would be impossible to get good results from psychotherapy when a patient is in a nervous state. From that standpoint, I believe that in cases of severe affective disturbances one can gain rapport with the patient and obtain some transference with removal of the disturbed affective component. After the first treatment, psychotherapy can be tried. No pathologic changes due to electric shock were observed. Kalinowsky stated that patients with obsessive-compulsive states should have twenty shock treatments. Some cases have been reported in which forty to sixty electric shock treatments were given without any obvious damage. The amount of postmortem material on patients who have had electric shock is very meager.

Reevaluation of Contraindications to Electric Shock Therapy. DR. MATTHEW T. MOORE.

The early enthusiastic application of convulsive shock treatment of mental illnesses, owing perhaps to indiscriminate and incautious use, resulted in numerous complications and occasional deaths. These unlooked-for, untoward effects led to a swing in the direction of conservatism, with resultant denial of treatment to many patients who would have benefited from this procedure. The severe convulsive reactions encountered with metrazol shock therapy and the early inexperience with methods of overcoming or subduing complications evidently produced the timidity with respect to contraindications which carried over to electric shock therapy.

A sufficiently large body of literature and experience has accumulated to provide a basis for reevaluating the indications and contraindications which, until recently, have been considered an unquestioned barrier to convulsive shock treatment; namely, acute infections and febrile diseases, advanced disease of the heart and kidneys, advanced age, bone atrophy in long-bedridden patients, pronounced spinal curvature and osteoarthritis, severe thyrotoxicosis, malignant growths, thrombophlebitis, advanced general arteriosclerosis, organic disturbances of the central nervous system and tuberculosis.

Some of these contraindications can now, in the light of experience and judgment, be eliminated from this category and greater freedom of use of this treatment be permitted. This applies to cardiovascular diseases with and without hypertension; advanced age; latent, arrested or even active tuberculosis; some cases of generalized arteriosclerosis in which a differential diagnosis between cerebral vascular involvement and involutional psychosis has not been established; organic

disease of the central nervous system, such as dementia paralytica; spinal curvatures, and osteoarthritis.

Six representative cases were reported. Such conditions as cardiovascular disease, with and without hypertension; pulmonary fibrosis secondary to tuberculosis; spinal curvature, and generalized arteriosclerosis were represented. No complications arose secondary to electric shock treatment, and in the main the results from the psychiatric standpoint were gratifying.

DISCUSSION

DR. BENJAMIN GOULEY: All can agree with Dr. Moore that in the earlier years of electric shock treatment many fears with regard to making worse serious organic disease did not have a basis in fact. One of the great fears in instituting treatment of this kind was that concerned with what such treatment might do to organic heart disease. Certainly, there has been little aggravation of preexisting heart disease with such treatment. Dr. Moore's paper has been matched by others, in which patients with various types of heart disease were not considered bad risks for shock treatment. I think that almost every patient of the Philadelphia Psychiatric Hospital has undergone electrocardiographic examination before treatment. After going over about 1,500 tracings, I can recall few instances in which organic heart disease, revealed by electrocardiographic examination, was made worse. I am under the impression that there has been 1 death as a result of shock treatment. Unfortunately, in that case electrocardiographic studies were not made. There arises the question whether the death was due to the electric shock treatment.

I am under the impression that the incidence of heart disease in the mentally sick has been exaggerated. I do not believe that there is as much heart disease in this psychiatric hospital as in a general hospital, and I doubt whether the shock therapeutist has to worry as much about the effects of his treatment as the surgeon does about such matters as anesthetics. There are, however, certain types of heart disease that might be looked on askance and shock therapy employed with reluctance. Certainly, I should not want to treat any one with acute or subacute myocardial infarction. Few such patients will enter an institution for the mentally ill. I have seen good internists much surprised when a patient of that type died and autopsy showed only myocardial infarction. Healed infarctions offer no barrier to treatment. A healed infarction in the anterior wall of the heart is more serious with respect to the risk of sudden death than is involvement of the posterior wall. In the presence of bundle branch block, especially what is called the left bundle branch variety, one has a sign that suggests conservatism in treatment. A patient with right bundle branch block is not a bad risk, no matter how loud the murmur he has nor how bad the electrocardiographic tracings may be. However, there are not enough such patients to warrant carelessness. One has to speak in terms of hundreds of cases before one can come to a satisfactory conclusion with regard to the more serious types of heart disease. A little caution will hurt neither the physician nor the patient.

DR. J. C. YASKIN: I feel that patients should not receive this treatment without first having an electrocardiographic examination. The medicolegal phase should not be disregarded. No treatment should be carried out without thorough physical, electrocardiographic and minimum laboratory studies.

DR. HERBERT H. HERSKOVITZ: About three years ago the society held a symposium on electric shock, and all of us listed the complications we had experienced; but we were generally agreed that patients with tuberculosis, cardiovascular disease, particularly arteriosclerosis, and bone deformities should not be treated. Since that time my associates and I at the Norristown State Hospital have not deviated much from those decisions. We have taken a chance with a few patients with moderate hypertension; but if cerebral arteriosclerosis is present, as found on examination of the eyegrounds, we will not give the patient electric shock. We do not worry about bone deformities because we use curare. We will take no

chances with tuberculosis, whether the lesion is healed or active. Although Dr. Moore presented 1 case of tuberculosis, the disease was not active. I know of a few cases in which healed lesions were transformed through electroshock into "galloping consumption."

DR. N. W. WINKELMAN: My colleagues and I are now in the midst of treating a young woman physician who received pneumothorax and electroconvulsive therapy simultaneously and is now receiving pneumothorax and insulin shock treatment. Apparently, there has been no change in her pulmonary condition. We are continuing treatment, and she is apparently thriving on it. Whether or not tuberculosis will prove to be an absolute contraindication is not as yet definitely determined.

DR. I. RODIS, Washington, D. C.: I treated a patient with moderately advanced congestive heart failure who was suicidal; it was a question of treating him with electric shock and taking a chance of killing him or letting him do away with himself. The family understood this, and nothing happened to him after the conventional administration of treatment. He was appreciably better. I have had occasion to treat several patients with auricular fibrillation and advanced myocardial degeneration as determined by routine electrocardiograms. Nothing happened. I do not now make electrocardiographic examinations as a routine.

DR. MATTHEW T. MOORE: I wish to thank the discussers especially, for they have brought up a number of points which, for lack of time, I did not present this evening. My intent was not to invite you to throw caution to the winds; on the contrary, this sample group of cases was reported to show that the former arbitrary and rigid contraindications could and should be relaxed, so that many patients could be receiving necessary treatment. Dr. Gouley mentioned the possible complications in treating patients with rheumatic heart disease. Only 1 case has thus far been reported in the literature in which an old endocarditis flared up after convulsive shock therapy. This case was reported by Ziegler, who stated that the condition subsided and the patient's mental state improved. Several patients with long-standing rheumatic heart disease have been treated without complications. Persons with advanced myocardial degeneration and decompensation obviously should not receive shock treatment. A review of the literature shows that many institutions are using convulsive shock therapy for patients with suicidal intent despite the presence of a serious cardiac condition. Kline and Fetterman, and Evans have treated a series of patients who had severe cardiovascular disease. Not only did these patients withstand shock treatment, but the psychiatric results were good.

I am fully in accord with Dr. Yaskin with regard to caution. My colleagues and I agreed that each patient should be studied carefully and individualized as regards the indications for treatment in the light of his physical state and the likelihood of his recovery.

With respect to Dr. Herskovitz' comment regarding tuberculosis, no conclusions can be reached from the one single case included in this report. However, the literature reveals that, although controversy still exists regarding this matter, most authors do not consider incipient, or even active, tuberculosis as a contraindication. Pacella cited 4 cases of latent and active tuberculosis treated with electric shock in which there were no complications and no reactivation of the pulmonary process. Smith reported the case of a middle-aged woman who had active bilateral pulmonary tuberculosis for several years. Fluid in the pleural sac and myocardial disease were present. She received a series of electric shock treatments; not only did she recover from her mental illness, but the pulmonary tuberculosis was said also to have improved.

Patients with disturbances of bony structures and joints can now escape without fractures or dislocations or may have them minimized, with the present method of proper splinting of the torso, limbs and head by means of four or five attendants.

A delicate point arises as to what constitutes advanced age. We treat all patients irrespective of age, treatment being determined by the person's physical

condition. We do not employ curare. It may interest those who are still using this drug that in a review of 11,000 cases in which electric shock was employed, Impastato and Almansi found 8 deaths, 4, or 50 per cent, of which occurred in patients who had received curare prior to treatment. It has been our feeling that this drug adds insult to injury by superimposing respiratory paralysis on the respiratory embarrassment incident to the shock treatment itself.

Histopathologic Study of an Early Case of Schizophrenia in Which Electric Shock Therapy Had Previously Been Employed. DR. N. W. WINKELMAN.

A young married woman of 22 was admitted to the Philadelphia Psychiatric Hospital on Jan. 16, 1945, was given the usual course of electroconvulsive therapy and was discharged as slightly improved on March 1, 1945. From her history it was learned that she had been born at full term and had weighed 3¾ pounds (1,700 Gm.) at birth. She did not walk until the age of 17 months and began to talk much later. As a child she was meticulous and liked to have her own way. She changed schools three or four times because of feelings of inferiority. She married at 19 and gave birth to her only child at the age of 22. After delivery her family and friends noted a complete change in her. She became apathetic and uninterested in her friends and careless in her personal hygiene. She gradually retreated from reality. The diagnosis was schizophrenia.

After her discharge from the hospital the patient seemed to adjust at home, but she worried about her husband, who was in the South Pacific. She committed suicide with gas on April 25, 1945.

Gross examination of the brain showed intense congestion.

Microscopic examination revealed the presence of scattered foci of either devastation or complete loss of cells throughout the frontal, temporal and parietal lobes particularly. There was no evidence of damage to the brain as the result of the electroconvulsive therapy. The carbon monoxide had produced no cerebral damage, since death had occurred within thirty minutes.

The question of a histopathologic picture characteristic of schizophrenia was discussed, with careful consideration of the two schools of thought, the one claiming that the changes observed in brains of patients with dementia precox can be duplicated in normal brains and the other believing that while specific changes do not occur with dementia precox there are alterations which are encountered uniformly.

It was concluded (1) that an assured and satisfactory histopathologic picture for dementia precox does not exist and (2) that the most constant change described in the literature, as in the case reported, is the presence of small focal cortical lacunas, from which groups of cells successively disappear.

DR. S. DEWITT LUDLUM: The schizophrenic person is a biologically poor organism; why should he not show biologic changes? Why did some patients have heart disease so early? They were in poor adaptability biologically. I see no reason that there should be any quarrel as to the functional or organic nature of schizophrenia. The two go together. If a person is not well put together, he falls victim to some disease.

DR. HERBERT H. HERSKOVITZ: I second Dr. Winkelman's remark that one should never make up one's mind regarding the cause of schizophrenia until the last word is written. In the first sentence of his summary Dr. Winkelman indicated that he does not believe that what he has described in his paper is the last word. Eventually the answer will be found. There is a pathology which also cannot be overlooked and must be studied just as intensely and just as thoroughly as Dr. Winkelman has studied the cells of his patient's brain. I refer to psychopathology.

DR. MATTHEW T. MOORE: During the early 1930's I was privileged to perform pneumoencephalographic examinations in 152 cases of various psychoses. Of

these, 71 were cases of schizophrenia. The diagnosis was definitely established, each patient having been seen by the staff and examined carefully before the diagnosis was made. The majority of the roentgenograms in the cases of schizophrenia showed a predilective atrophy of the parietal lobe, with a lesser degree of atrophy in the frontal and occipital lobes. This work has been repeated elsewhere, with the same findings. This week I sectioned the brain of the very first patient on whom I performed pneumoencephalographic studies in 1930. The films in her case showed the type of atrophy just mentioned. On gross inspection her brain revealed definite atrophy of the cerebral gyri. Section of the brain showed definite shrinking of the white matter. The controversy as to whether schizophrenia is a functional disorder or has an organic background still rages. It is generally known that until the latter part of the nineteenth century dementia paralytica was considered a functional disorder, and it was not until the treponema was found in the brain substance and the characteristic pathologic picture of dementia paralytica was established that the organic nature of the disease was accepted. Mott, in the early part of the century, showed that many brains of schizophrenic patients had hypoplastic vessels at the base. The work of many investigators, including Dr. Ludlum, indicates the structural and biochemical disturbances which seem to characterize persons with schizophrenia. The fact that no specific change in the cells of the brain can as yet be demonstrated in these cases does not militate against the assumption that some morphologic or biochemical change may exist in the brain substance. In any event, it is essential to have an open mind regarding such problems. Dr. Winkelman's offering this evening is deserving of credit in that it is a probing study and will serve, I am sure, as a steppingstone to a better understanding of this intriguing, and as yet elusive, subject.

MAJOR M. M. KESSLER, M.C., A.U.S.: I am emboldened to make a few remarks which are contrary to the theory presented, because it is generally accepted that schizophrenia is a functional nervous disease without a known pathologic basis. Through significant researches the general conclusion has been reached that the brain of a schizophrenic person presents no demonstrable pathologic change, either grossly or microscopically. On the other hand, there are cases of schizophrenia in which the disorder is superimposed on an underlying organic disease. Schizophrenia can occur with mental deficiency. It is then called a psychosis with mental deficiency. One does not conclude from such a combination that any pathologic condition observed in the brain of a mentally deficient person is the cause of schizophrenia.

In the case presented the patient weighed only 3¾ pounds at birth, indicating that there may have been some abnormality in the child from the time of birth. This was confirmed by the report of general retardation in the early developmental years. Other complicating factors disturb the clarity of this case as one demonstrating the pathologic changes of schizophrenia. Not long before the patient's death she received insulin hypoglycemia and electric shock therapy. These are known to cause an encephalopathy. An additional confusing factor is that the patient committed suicide with carbon monoxide. The history is not clear as to how long the patient lived during the exposure to gas. The anoxemia attendant on this means of suicide could easily result in pyknosis of brain cells and attenuation of cell processes. The reduction of brain cells in certain areas of the brain could be part of an old process which has been present since birth. I feel, therefore, that the author's conclusion must be accepted guardedly. It may well be that in this case the schizophrenic psychosis was merely superimposed on an encephalopathy of unknown origin.

MAJOR THEODORE LIDZ, M.C., A.U.S.: Major Kessler's discussion has raised a vital point. It affects not only the paper which has just been read but attitudes which have been prominent throughout the evening. It permits, if it does not lead to, the assumption that some organic means of cure must be found. It fosters the concept that unless some physical measure can be adopted the patient is

incurable. It is well to remember that patients with neuroses and psychoses similar to those presented here improved and recovered before shock therapy was introduced.

To continue to search for questionable changes in the cortex when another, very gross pathologic condition calls to any careful listener seems to me to lead in the wrong direction. Listening day after day to the histories of schizophrenic patients, as one does at the Army psychiatric centers, reveals striking abnormalities of family setting and social development of the individual that are real, factual and concrete, even though they exist only in historical perspective. One does not have to peer through a microscope at a brain which may have been damaged by several other traumas to find a pathologic process in schizophrenic patients.

It may also be revealing to come to a military hospital where soldiers arrive with records of typical schizophrenic reactions and recover promptly; or to see, as I have had the good fortune to do, patients I have sent home from India whom I thought would never recover because of behavioral patterns that seemed rigidly fixed in negativistic or paranoid constellations, appear totally changed and apparently well after several months in the United States.

At the Army general hospital where we are stationed my colleagues and I have month after month seen approximately 70 per cent of the psychotic patients, including those with schizophrenia, return home after several months of hospital care without shock treatment. I assure you that we have not been able to offer them elaborate treatment, much as we should like to, because of the pressure of work. They receive good care, an active program that keeps them well occupied, but primarily consideration and respect. If the change from the jungle to the United States, from despair and frustration to consideration and social existence, can produce a change so profound within a few months, one gets a different impression of schizophrenic reactions and of what may be making these patients ill.

DR. N. W. WINKELMAN: I am in thorough accord with Dr. Ludlum about the poor structural makeup of the schizophrenic patient. I believe that schizophrenic persons are born, not made. The patient I reported weighed 3¾ pounds at birth. Her whole life showed inadequacy, not mental deficiency. She got along in school with her studies, but not with her companions. After the stress and strain of childbirth, she "broke" and a true schizophernia developed. She committed suicide with gas. One can disregard the histopathologic changes due to the carbon monoxide because she died within thirty minutes. Death in cases of this sort is a "blood death," due to deprivation of oxygen; it is not a "brain death." Had this patient lived on for twenty-four to forty-eight hours, we should then have had recognizable cerebral damage which would obscure and confuse the changes which we believe may result from the schizophrenic process itself.

NEW YORK NEUROLOGICAL SOCIETY AND THE NEW YORK ACADEMY OF MEDICINE, SECTION OF MEDICINE AND SECTION OF NEUROLOGY AND PSYCHIATRY

Franklin M. Hanger, M.D., *Chairman, Section of Medicine, Presiding*

Joint Meeting, Nov. 20, 1945

Intravenous Administration of Histamine in Treatment of Migraine. DR. WILLIAM A. THOMAS and DR. STUYVESANT BUTLER, Chicago (by invitation).

Histamine (decarboxylated histidine), released by allergic reactions, remains only momentarily in the circulation and is taken up by the tissues. There is no sensitization to histamine in the anaphylactic sense, as it is nonantigenic; but in persons with lower tolerance to histamine this substance reaches shock organs (skin, bronchial tubes, arterioles and capillaries), causing characteristic responses.

Migraine is thought by the authors to be such a reaction and has been treated by long-continued intravenous injections of a solution of histamine in an effort to increase tolerance to the substance.

Seventy-five patients with severe, indisputably migraine headaches were given 1 mg. of histamine base as 2.75 mg. of histamine phosphate in 500 cc. of isotonic solution of sodium chloride in the form of an intravenous drip. Results showed increasing tolerance and satisfactory results, with permanent complete relief in 30 patients, temporary complete relief in 11, partial relief in 25 and no relief in 9. The authors suggested even longer-continued (twenty-four hour) injections for patients failing to respond satisfactorily to the shorter, four to eight hour, injections.

This paper was published in full in the March 1946 issue of the *Bulletin of the New York Academy of Medicine*, pages 125 to 136.

DISCUSSION

DR. STANLEY COBB, Boston (by invitation): It is obvious that men who are able to give complete relief in 40 per cent of cases of migraine headache have made a real advance, and I think the speakers of the evening are to be congratulated on that score alone.

I should like to ask about some particulars. In the first place, I am a little skeptical about the relationship of Ménière's disease (in the strict sense of the word) to migraine. I think that there is a relation between migraine and spells of vertigo and dizziness, but not classic Ménière's disease. Such a distinction is perhaps academic.

Then I should like to ask the authors concerning their statement about the allergic response. They spoke of it as a widely accepted idea that migraine is an allergic response to histamine. I should not say that the idea is widely accepted, and I think from their later words they do not accept it themselves. If migraine is considered, not as an allergic response, but only as a lowered tolerance to histamine, it is easier for me to understand.

The observations on the vessels of the eyeground interested me greatly, for I should think that when they were giving histamine intravenously they would have seen vascular dilatation. In experiments that Dr. Wolff and I carried out in 1928 histamine gave a widespread dilatation of all the cerebral vessels. Moreover, I had thought that histamine headaches were caused by a wide dilatation of the cerebral vessels.

I wonder why this remarkable effect is produced by the intravenous administration of histamine and none to speak of by the subcutaneous method. Is there any explanation for that?

DR. WILLIAM A. THOMAS, Chicago: I shall answer Dr. Cobb's last question first, that is, the superiority of intravenous injection to the subcutaneous method. I had hoped to make that clear, but I fear I did not. Histamine, regardless of the source of origin, whether injected subcutaneously or intravenously, or produced by some other mechanism, such as heat or cold, remains in the circulation momentarily, no longer. If a constrictor is placed about the upper part of the arm, histamine is formed in the lower part of the arm, and during the time the constrictor is there blood withdrawn from the vein will be shown to contain histamine. If the constrictor is removed, histamine immediately disappears from the circulation. It is taken by the cells so rapidly that there is none circulating. It has been our idea that if one wishes to increase the tolerance of a patient to histamine, rather than give the substance in injections two, three or four times a day, with a brief exposure, necessarily a limited one, because one cannot give doses that will produce shock of any type, one should provide long-continued exposure by giving histamine intravenously for six, ten or twenty-four hours, as fast as the patient can take it. We have found that the patient's tolerance can be raised from taking 3 or 4 drops a minute, and a total of 40 to 50 cc., to 10 drops a minute, and a total of 100 cc., and eventually to the full dose, 1 mg. of histamine base.

I hope I have not misstated what we mean by histamine cephalalgia. We believe that headaches which are paroxysmal and unilateral may be a histamine cephalalgia. As I understand it, there is a great deal of discussion as to whether true histamine cephalalgia is due to vasodilatation or to vasoconstriction. We have to deal with many of the manifestations of histamine reactions. The rate at which histamine is given determines entirely what happens. It can be given so slowly that one gets the histamine reaction—the flushing of the face, then of the neck and then of the shoulders—but at the same time there is a vasoconstriction of the lower extremities with a decrease of body temperature as much as 5 degrees (Fahrenheit). The reason I have been so emphatic against the use of histamine as a skin test is the great variability of the reaction. The response to histamine depends entirely on the balance of forces between the vasoconstrictor and the vasodilator mechanism. A reaction before a meal or before ingestion of alcohol will be slight, and that after a meal and after ingestion of alcohol will be great. If two similar doses are injected in the two arms and a blanket is placed over one area, this area will be four or five times as large as the other. An outstanding fact to be considered is that the cutaneous reaction is minimal in brunets, large in blondes and maximal in red-headed persons. Therefore, where the histamine reaction takes place, whether it involves the vessels of the internal carotid artery or not, depends on the rate at which the substance is given, and in patients with migraine one cannot give it fast.

We had no intention of relating Ménière's syndrome to migraine; it was only after Rainey (*J. A. M. A.* **122**:850 [July 24] 1943) had treated Ménière's syndrome unsuccessfully with subcutaneous injection of histamine that he found he had better results with the intravenous method; I simply stated that he confirmed our point that the intravenous method is superior.

As far as the question of allergy is concerned, I was certain we were going to run into some problems. We came here to discuss the intravenous treatment of migraine with histamine, and not these other ramifications. If the thesis is correct, the $64 question is where the histamine comes from; and I do not know whether it is allergic or not. We have no intention of stating that it is; I meant to say that it is fairly generally believed that such is the case. We do not subscribe to the idea entirely.

Dr. Harold G. Wolff: I should like to discuss this interesting and important contribution to the management of migraine headache from two points of view: first, that of the mechanisms of the preheadache phenomena and of migraine headache, and, second, that of the management of migraine headache. The preheadache phenomena constitute the part of the migraine attack itself that is nonpainful and consists of visual, and sometimes sensory, disturbances. It has been deduced from evidence obtained in patients that cerebral vasoconstriction primarily within the cranial cavity is responsible for such preheadache phenomena. As far as has been observed, there are no painful components during this phase of the attack. The painful phase is associated with vasodilatation and is related to changes in the amplitude of pulsations of cranial arteries, chiefly the branches of the external carotid artery. Whether the headache stems entirely from structures outside or inside the head can be dismissed for the moment. It is important to emphasize the difference between the preheadache and the headache phase of migraine, for there is no experimental evidence that vasoconstriction inside the head gives rise to pain. The headache phase of migraine has to do with vasodilatation.

If ergotamine tartrate is given during the early part of the painful phase of a migraine attack, it constricts the cranial vessels, chiefly the branches of the external carotid artery, and to a less extent the branches of the internal carotid artery, and is thus successful in eliminating the headache. If it is given late, it usually constricts the vessels less rapidly and less completely, and perhaps not enough for therapeutic purposes.

It was postulated that after the sustained arterial dilatation of a local artery of the head, there occurs a transient change in the structure of the arterial wall,

namely, thickening or edema of the muscular and adventitial structures. Sections of blood vessels of patients with intractable migraine headache were removed while the temporal arteries were being tied off for the relief of pain. In these sections there were found some hints of thickening of the walls, but suitable controls were not available. Experiments were then carried out on the arteries of cat ears. These were studied after prolonged vasodilation produced by infusion for two hours of 10 cc. of mammalian Ringer's solution containing a vasodilator agent. The dilated arterial walls were compared with the arterial walls of a control ear by means of serial sections. Measurements demonstrated thickening of the arterial walls of the infused ear. Also, the vasoconstrictor agent, ergotamine tartrate, was found to be less prompt and less effective in constricting arteries with such thickened or edematous walls than arteries with normal walls.

Similar changes in arterial walls of patients during long migraine headaches may be the explanation for the rigid, pipelike texture of the arteries; the steady, aching pain, and the tenderness of these structures. Also, these changes may explain the decreased ability of ergotamine tartrate to reduce the intensity of prolonged headache.

There is a second mechanism of pain during the migraine attack which should also be considered; it involves sustained contraction of the muscles of the head and neck. Pain in the head from any cause induces secondary contraction of these muscles, which when maintained becomes in itself a source of pain. Such painful contractions may outlast for some time the primary cause of the contraction, i. e., cranial vasodilatation. This affords an explanation of the failure of ergotamine tartrate to produce relatively prompt relief in some patients who have a major muscle component in their headaches.

The chief consideration, however, and the question so far unsatisfactorily answered, is what makes the cranial vessels dilate—is histamine the agent that causes the dilatation that is so painful? What is the evidence for the role of histamine to date? Important pieces of evidence have been presented by von Storch and by the speakers of the evening. They have observed that in some persons with migraine the injection of small amounts of histamine will more readily induce a headache than in the average person not susceptible to migraine. That is interesting but not conclusive,, because in some persons with migraine the ingestion of small amounts of alcohol also precipitates headache. One must therefore wait for more conclusive evidence that histamine is the agent causing vasodilatation in the painful phase of the migraine attack.

What is the bearing of all this on treatment and the prevention of migraine attacks? Certainly, the evidence as given tonight indicates that the administration of histamine intravenously in precisely the manner described has dramatic effect. But the interpretation of the results of this method of treatment is difficult. It is easy to observe the success or failure of an agent in terminating an individual attack of headache, but in an illness that is so unpredictable in terms of the next attack, and in such a complicated situation as migraine headache assumes in terms of the patient's life, it is not so easy to evaluate what is going to prevent a headache a week or a month hence. It is interesting, however, that any planned regimen reassures the patient and gives him a conviction of being cared for, which is important in the treatment of migraine.

For example, we have a patient, a woman aged 44, with a history of migraine over many years, who was having an incapacitating headache once or twice a week during July and August. She came into the clinic at the end of August and was given lactose pills and nothing else, except for the assurance that she did not have a cerebral tumor or other serious illness. She was told to take her pills three times a day. During September and October she had no headaches for a three week period, and then infrequent, mild headaches of short duration. That is characteristic: a short-lived effect while the patient is in contact with the physician and with the administration of a symbol of therapeutic significance.

The second case is a little more complicated. The patient was a man aged 48 who had one or two headaches a week during 1936, 1937 and 1938. I had three

interviews with him in 1938. It is not important to discuss what was said except that he was reassured as to the nature of his headaches and his emotional attitudes were considered. Thereafter his headaches stopped until the spring of 1939, when he had a few; and again in the spring of 1941 he had a few attacks. I interviewed him once, and his headaches stopped. He had none during the remainder of 1941 and during 1942 and 1943. In the fall of 1944 he got into a frustrating situation of inactivity in his Navy post, which precipitated a great many headaches, almost daily for a while and always the same. Then an able young physician treated him by means of subcutaneous injections of histamine in the manner described by Horton (*J. A. M. A.* **116**:377 [Feb. 1] 1941), and this therapy was painstakingly carried out. The headaches then stopped completely but returned again after a few days. He was given more treatment and had no headaches until three months later. He was again given a series of subcutaneous injections of histamine, but the headaches continued throughout the first three months of 1945. I saw him again on April 1, and we discussed matters concerning his attitudes, which were of first rate importance to him; and he has had no more headaches to date (a period of six months). If such is the natural history of patients with migraine, it is evident how exceedingly difficult it is to draw any inferences concerning the effect of a specific therapy. This does not sanction a nihilistic point of view but indicates the difficulty in drawing inferences.

Concerning the percentage of successful effects with various therapies, it is interesting that if one picks at random three forms for which statistics have been given the results are not dissimilar. For the treatment of Balyeat, who managed his patients with migraine by taking away certain food substances, the results were practically the same as those of the speakers this evening: 30 per cent excellent, 30 per cent good, 20 per cent fair and 20 per cent failures. Pfeiffer, Dreisbach and Roby (*J. Lab. & Clin. Med.* **29**:709-714, 1944), who gave a mixture of calcium lactate and potassium chloride to 150 patients over a period of three years, reported results as follows: 24 per cent excellent, 39 per cent good, 27 per cent fair and 10 per cent noneffective. In other words, they achieved over 70 per cent good and excellent results with an entirely different method of management. In my own series there are 58 patients, of whom 28 per cent had no recurrences in a period of several months to five years; 33 per cent had some headaches, but infrequently and of less intensity; 18 per cent had some improvement, but not very satisfactory, and about 20 per cent had no improvement. The management consisted in reviewing the patient's problems, indicating the nature of migraine, pointing out certain dominant drives in the patients and showing the need for changed attitudes. With this type of therapy I got about the same results as those for the two treatments cited and about the same results as did the speakers of the evening. These statistics on the success of other types of therapy do not indicate that histamine is not the specific agent in causing or preventing migraine headaches. By presenting them, I wish to emphasize again that it is exceedingly difficult to draw inferences, and I do not think that the evidence presented tonight has settled the question as to what causes the painful dilatation of the cranial vessels in migraine headache and whether histamine is the specific therapeutic agent.

DR. MILES ATKINSON: I have been particularly interested in the question of Ménière's syndrome, as you probably know, and I have found that a fairly large number of patients with migraine in the early years of life had Ménière's syndrome in their later years. I do not say by any means the major proportion, but a fairly large number. I presented this material in the paper to which Dr. Thomas referred (Diagnosis and Treatment of Ménière's Syndrome, *Arch. Otolaryng.* **37**: 40 [Jan.] 1943), and it has been my concept that this group of patients possesses a primary vasoconstrictor mechanism, such as Dr. Wolff has described and demonstrated, which in the early years produces migraine—the primary vasoconstrictor, or preheadache, phenomena and the secondary vasodilator, or headache, phenomenon. In the same way, in the case of Ménière's syndrome there is a primary vasoconstrictor group. In this vasoconstrictor group of Ménière's syndrome,

which is the major group, the same thing happens: There is a primary vasoconstrictor disturbance in the inner ear which causes vertigo; then, when the vessel relaxes, the patient gets the aftermath of unsteadiness and quite frequently headache, not migraine headache, not the typical unilateral headache, but headache of one sort or another. I have become so convinced of this that I am accustomed to say that a migraine is Ménière's syndrome in the brain and Ménière's syndrome is migraine in the ear. It was this observation which led to my interest in migraine and to my suggestion that it might be a good plan to try and prevent the primary vasoconstrictor mechanism in migraine by producing vasodilatation; and, as I have been accustomed to use nicotinic acid, not as a vitamin but as a vasodilator, I suggested it might be used to prevent attacks—not to cure the attack in being but to prevent its onset. I published a small series of cases (*Ann. Int. Med.* **21**:990, 1944), to which Dr. Thomas referred, in which it did seem to have some good effect. I also suggested that histamine might do the same thing, for my view of histamine in connection with Ménière's syndrome and migraine is that it acts not in any recondite manner, but probably simply as a vasodilator. I should like to ask Dr. Thomas a question which has been on my mind for some time. I have had no great experience in treating migraine—I just pick up the cases as I find them, and I do not see a great many. I have had no personal experience in treating migraine with histamine, but I have had experience in treating patients with Ménière's syndrome myself and in seeing patients who have been treated by others with intravenous injection of histamine. It has been my experience that it is again the vasoconstrictor group in which one gets a good initial result in relief of Ménière's syndrome, which, as I say, is in my view migraine in the ear; that they will get relief of symptoms for a varying period after the first course of treatment, and that sometimes when they get a relapse a second course will help them, but often a second course will not help them. They get no effect from it at all. I can think of several cases in which no improvement has occurred with a second course of intravenous injections of histamine, and I have found it seems to make the headaches more resistant to the action of nicotinic acid. I should like to ask Dr. Thomas whether he has had a similar experience in treatment of migraine.

DR. WILLIAM A. THOMAS, Chicago: I do not believe that we differ from Dr. Wolff in any significant way. It has been my purpose to make myself familiar with his work. I agree with his concept that anxiety and rage, that is, emotional disturbances, are frequently causes of attacks of migraine, and I am sure that all have had about the same results in treating migraine. Twenty years ago, with Dr. Joseph Miller, we started treating a series of patients with very severe migraine; we gave them each morning a small wineglassful of grape juice on which we dropped 30 drops of castor oil and followed that with calcium lactate during the day. A large number of these patients had dramatic relief. Dr. Wolff has indicated this in his report on Dreisbach's patients, with use of calcium lactate. The difference of opinion exists, of course, very largely in whether the vasoconstriction and the vasodilatation follow one another and whether they are caused by the same mechanism. We are inclined to agree with Dr. Wolff that branches of the external carotid artery and the extracranial nerves are chiefly concerned in headache and that those vessels are in a state of vasodilatation when the headache appears. Another point in confirmation is that when one is able to test for histamine in the blood, regardless of the avenue of its entrance, histamine has disappeared by the time the headache begins.

There are two other points which might be brought out in relation to Dr. Wolff's discussion. One is that in working with Drs. Ivy and Grace Roth, of the Mayo Clinic, it was discovered that histamine has a tremendous capacity for lowering the threshold of pain. Ivy has a pain machine and has found that most patients who receive histamine suffer a great deal more from the headache than does a person with a similar headache not caused by histamine.

I cannot answer Dr. Atkinson's question. We have had patients, just as he reports, who have had some primary relief from intravenous injection of histamine,

as he has in cases of Ménière's syndrome and then had no relief from subsequent treatments, and we do not know the mechanism. I should like to ask whether Dr. Atkinson knows why the primary vasoconstriction he visualizes causes the pain; or is the total mechanism, with the primary vasoconstriction and the secondary vasodilatation, responsible?

To come back to Dr. Wolff's question about histamine: We do not know that is the only cause. We do know these attacks are brought on by emotional and vasomotor instability, as well as by thermal reactions. One of the best explanations I know was suggested when Dr. Butler and I first gave this paper in Chicago. It was widely discussed—the type of migraine, the attacks and the frequency—and one person asked, "Can you tell me why there are so many migraine attacks on Sunday, when the patient should not be subject to strain, when it is not a matter of dissipation the night before?" and we were able to answer, "Because so many hot baths are taken on Saturday night!"

DR. STUYVESANT BUTLER, Chicago: I have a few words to say regarding these comments.

We have given histamine, Dr. Wolff, to a number of so-called normal persons in an attempt to determine whether there is a difference in the secretion of hydrochloric acid in the stomach of ulcer-bearing patients and normal persons and to find whether there is a similar reaction to that found with caffeine. We have given histamine very rapidly to these subjects, much more rapidly than we can give it to patients with migraine. We have obtained no headaches whatever, in spite of the fact that they have had the other signs—the severe flushing of the face, for example—and sometimes have had urticaria, even when they had no history of it. It may be that there is something about these patients that makes them have migraine, whereby they specifically get this dilatation of the branches of the external carotid artery, while the normal, nonmigrainous, person does not.

I am much interested in Dr. Wolff's reports of the psychotherapy of these patients. We have seen a number (I personally have seen 5) who have at some time attempted suicide because of the severity of the attack and have seen 3 narcotic addicts who had had every possible type of therapy for their headaches before (and I do not believe that they took to narcotics unless the headaches were very severe), and I do not believe that psychotherapy could have helped them. In our series, the cases of greatest severity were the ones in which the greatest percentage of relief was obtained.

In regard to Dr. Atkinson's comments, we have been wondering whether the fact that one of the products of the metabolism of nicotinic acid is histamine may have something to do with the results that he has described; in other words, a continuous giving off to the body of histamine taken in the form of nicotinic acid.

DR. HAROLD G. WOLFF: It seems to me that this important work ought to be put into shape so it will be available to every one immediately. It is basic. Would it be possible for the investigators to give an equivalent amount of salt or dextrose to alternative patients with headaches of the same nature, magnitude and severity, under the same set of conditions in their laboratory, as when histamine is administered? I think if the results obtained in the 75 patients treated with histamine could be balanced with results obtained from such controls that it would give much more evidence as to the specific action of histamine.

Book Reviews

Les gliomes infiltrés du tronc cérébral. By Georges Guillain, Ivan Bertrand and Jean Gruner. Price, 450 francs. Pp. 286, with 119 illustrations. Paris: Masson & Cie, 1945.

If evidence is necessary of the outstanding achievements of the French scientists, it is furnished by the magnificent book of Guillain, Bertrand and Gruner, written in the spirit of their masters Charcot and Marie, whom all neurologists may proudly call their masters. A surprising fact is the presentation of this first French postwar book in the usual, fine manner of the Masson publishers.

The book discusses those not infrequently encountered infiltrating gliomas of the brain stem (5 per cent of a series of 250 tumors of the brain) which frequently occur in childhood and present diagnostically misleading signs. Headache, though present, does not indicate that the intracranial pressure is increased with these growths. Papillostasis is absent in 60 per cent of cases. These tumors are accompanied with fever, suggesting the diagnosis of encephalitis or of acute multiple sclerosis, and the signs (hemiplegia or paraplegia associated with cerebellar signs) are not contradictory to such a diagnosis, particularly since sensory disturbances are rare and nystagmus, dizziness and speech disturbances are frequent. There is a remarkable abnormal position of the head. Of the cranial nerves, the anterior group (third, fourth and fifth) are rarely affected; the posterior group (sixth to twelfth) are frequently involved. The course is acute in many cases (two to four months or more) but rarely longer than two years. This fact, together with the fever and the absence of a greatly increased intracranial pressure, accounts for the diagnostic difficulties.

Excellent pathologic descriptions accompany the clinical part of the text, and 119 pictures illustrate the manifold kinds of tumors encountered in the 12 cases of the authors. There may be an isomorphous, nondestructive or eccentric gliomatosis, or the tumor may be rather circumscribed. These gliomas consist principally of unipolar spongioblasts of a pseudoneuronophagic, infiltrative type, most prominent subpially and perivascularly. However, all types of gliomas are represented. Some appear as nodules, indicating a polycentric growth. Surprising in cases of these tumors is the relative intactness of the gray matter, contrasting with the demyelination in the infiltrated areas. The relative intactness of the axons explains the lack of secondary degeneration.

Some predisposing factor, some *faiblesse* of the glia, may aid in the development of the tumor. Of great interest is the discussion on the relation of these infiltrating tumors to some encephalitides, particularly the blastomatous form of Schilder's disease, and to the gliomas in Recklinghausen's disease, to which they have many similarities.

The only therapeutic measure recommended is palliative trepanation, which apparently prolongs the life of the patient.

To their own 12 cases the authors added 80 cases from the literature, citing them in a way that greatly increases the value of the work. It is noteworthy that in the bibliography prior to 1920 one finds two American scientists only (Weisenburg and Spiller), whereas in the bibliography of the past twenty-five years more than forty American names appear, evidence of the great interest in this field of neurology in the United States.

In this book, the authors have attempted to employ a new approach to the complicated problem of the tumors of the glioma group which may help solve some questions of interest to the neurologist.

Manual of Diagnosis and Management of Peripheral Nerve Injuries. By Lieutenant Colonel Robert A. Groff, M.C., A.U.S., and Lieutenant Sara Jane Houtz (P.T.) A.U.S., with introduction by I. S. Ravdin, M.D. Price, $6. Pp. xii+ 188, with 111 figures. Philadelphia: J. B. Lippincott Co., 1945.

The high rate of peripheral nerve injury in the second world war presented both a challenge and an opportunity to clinical medicine and medical research, in a field which has been relatively inactive since the first world war. Accordingly, several new books on peripheral nerve injuries have appeared within a short time of each other.

The manual under review was designed by its authors "to provide the physician and physical therapist with a concise text containing the essential facts for the understanding, identification and management of injuries to the peripheral nerves." They may be said to have fulfilled this task well if it is borne in mind that the book is designed for "those individuals with little or no previous experience who have had the problems of nerve injuries forced upon them." To the specialist in physiology, neurology or neurosurgery and to advanced students in these subjects the manual is less valuable, except for its emphasis in the first part on the physiologic basis of nerve reactions under normal and pathologic conditions.

In its nine chapters, which total less than sixty pages, part I, on nerve injuries, discusses readably and swiftly the general principles of the anatomy, physiology and neurology of nerve lesions. It contains brief sections on the reaction of injured nerves, phenomena of recovery and regeneration, operative treatment and post-operative care, including the treatment of causalgias. Some unbalance is introduced through the relatively long sixth chapter, which deals with neurosurgical treatment. Since in peacetime it would hardly be desirable for any but neurosurgeons to carry out the operations discussed therein, much of the chapter, dealing, as it does, briefly with preparation of the patient, anesthesia, position, surgical preparation and instruments and, in about 8 pages, with the technic of exposure and repair, appears to the reviewer to be disproportionate. The authors devote a relatively large space (nearly two and one-half pages and a figure) to a modification of the Tarlov plasma glue technic, which has been used successfully by the senior author, but no mention is made of tantalum sutures or cuff.

The first part is illustrated with twelve drawings. The value of the principal feature which figure 1 illustrates, the composition of a spinal nerve, becomes greatly minified because an added attempt was made to show the spinal cord in relation to a vertebra. This figure contains errors both in the drawing and in the legend.

Part II of the manual is devoted to the details of clinical examination of peripheral nerve injuries. It is introduced by a short chapter on muscle isolation and the principles and general rules of muscle testing. It contains a brief discussion of functional substitution. The remainder of part II is essentially an atlas, with a minimum of text, dealing with functional examination of regions innervated by the cervical plexus, the brachial plexus, the thoracic nerves, the lumbar and sacral plexuses and the cranial nerves. A highly schematic diagram is included with each section to show the distribution of the nerve groups. Offsetting the defect of such schematic diagrams are seven good, large scale anatomic drawings, showing dissections of the major nerves, muscles and vessels of the face, arm and leg. The detail illustrations, of which there are nearly one hundred, are line drawings and action diagrams, which should, as the authors intend, furnish a guide to the physical therapeutist for the administration of specific muscle exercises. To the reviewer they are not as satisfying as photographs of illustrative cases.

A brief bibliography and a good index conclude the manual, which should prove valuable to the physical therapeutist and as an introductory book for clinical practice.